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INFLUENZAL MENINGITIS, WITH ESPECIAL REFERENCE TO ITS PATHOLOGY AND BACTERIOLOGY *

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Influenzal meningitis, on account of its rarity, has attracted little attention in medicine. However, as the condition is becoming better known, and especially since improved diagnostic methods have come into more general use, the number of cases reported from various countries is increasing each year and evidently they will soon cease to be uncommon. There has been a wide difference of opinion in regard to the significance of *B. influenzæ* in infections, especially in ordinary influenza or "grippe." This is chiefly due to the fact that epidemics occur which in their clinical features are practically identical, but which appear to be caused by a variety of organisms in the respiratory tract. Whatever may be the outcome of this controversy, the occurrence of influenza bacilli in pure culture in cases of meningitis demonstrates conclusively that this organism may be highly pathogenic and therefore its presence in throats, sputa, etc., should not be regarded with indifference.

Recently the literature on the subject of influenzal meningitis has been analyzed by several writers. Adams,[1] Cohoe,[2] Cohen,[3] and Wollstein[4] have collected the cases and discussed their more important features. It is difficult to state just how many cases should be included as primary influenzal meningitis, because mixed infections occurred in a considerable number. It is undoubtedly true, however, that in many if not in all of the cases of mixed infection the influenza bacillus was the primary invader of the cranial cavity, for the reason that cocci which were found associated with influenza bacilli are very common secondary invaders, whereas influenza bacilli are rarely found as such. The cases are widely distributed, occurring in various countries in Europe and America. In general they may be said to be sporadic, there being no tendency for them to occur in epidemics; nor is there any clear associ-

*From the Pathological Laboratories of Rush Medical College.

1. Adams: Arch. Pediat., 1907, xxiv, 721.
2. Cohoe: Am. Jour. Med. Sc., 1909, cxxxvii, 74.
3. Cohen: Ann. de l'inst. Pasteur, 1909, xxiii, 273.
4. Wollstein, M.: Am. Jour. Dis. Child., 1911, i, 42.

ation between their occurrence and epidemics of influenza or grip. It is a disease confined very largely to children under 1 year of age. Five cases have occurred in individuals over 20. The mortality is about 90 per cent.

The reports of Ghon,[5] Fraenkel,[6] Dubois,[7] Cohoe,[2] Cohen[3] and Wollstein[4] give the most complete bacteriologic and histologic studies that have been made. More than half of the cases have come to autopsy.

Recently[8] I reported the occurrence of this disease in twin brothers, with autopsy and bacteriologic findings in one. Since that time five other cases have been met with in Chicago, making seven in all, five of which have been examined post mortem. These cases are here recorded, special attention being given to the pathologic anatomy and bacteriology of the disease.[9]

CASES 1 AND 2.—Twin brothers were born by a healthy mother at full term in a normal condition. Five days later both infants became ill with symptoms of acute enteritis, associated later with muscular twitchings, cyanosis, stupor, and temperature ranging from 100 to 104 F. One child died on the fourth day of the disease and the other died on the seventh day, both having run almost identical clinical courses without definite meningeal symptoms. Autopsy was permitted in the first case only and was made by Dr. LeCount.

Anatomic Diagnosis.—Acute purulent leptomeningitis; acute parenchymatous degeneration of the heart, liver and kidneys; acute swelling of the spleen; multiple ecchymoses of the pleura and thymus; acute catarrhal gastro-enteritis.

B. influenzæ was found pure in smears and cultures of the meningeal exudate, cerebrospinal fluid and peritoneal fluid. In the heart's blood were a few *B. coli* but no influenza bacilli. In the cerebrospinal fluid were numerous cells, 80 per cent. of which were polynuclear leukocytes and both within and without these cells were enormous numbers of influenza bacilli.

Over the entire convex surface of the brain were well defined areas of greenish-yellow purulent exudate, irregular in shape and from 1 to several sq. cm. in size and 1 to 5 mm. thick. At the base, especially in the region of the optic chiasm and the pons, and along the larger blood-vessels, the deposit was more abundant and diffuse. No pathologic change was present in the nasal or tympanic cavities.

Microscopically the exudate was made up largely of polynuclear cells, there being also in places mononuclear and phagocytic endothelial cells in considerable numbers, but very little fibrin.

CASE 3.—Infant girl aged 13 months, admitted to nursery of Chicago Maternity, Sept. 22, 1908. The child did rather poorly at first, but later gained. On December 1 she contracted a cold, which was prevalent in the nursery. The temperature remained normal and appetite good until December 6, when the child showed signs of serious illness, the temperature rising to 101.6 F. The chest-findings suggested bronchopneumonia. The following day the symptoms became worse, the temperature rose to 103 F., and the child was isolated and treated for pneumonia. She was restless, coughed some and cried a good deal. The stools

5. Ghon: Wien. klin. Wchnschr., 1902, xv, 667.

6. Fraenkel: Ztschr. f. Hyg., 1898, xxvii, 315.

7. Dubois: Thèse de Paris, 1902, No. 49.

8. Davis, D. J.: Arch. Int. Med., 1909, iv, 323.

9. A short summary of these cases is given in Tr. Chicago Path. Soc., 1910, viii, 39, the pathological specimens having been shown to the Chicago Pathological Society in joint meeting with the Chicago Neurological Society, March 14, 1910.

remained normal and she took her food fairly well the first six or seven days of the illness. The child showed from the first a disinclination to have her head moved, and resisted handling. No retraction of the head was noticed until after the ninth day of her sickness, though she showed from the beginning slight rigidity of the neck muscles. On the seventh day the fever remained below 101 F., going down to 99.4 F., and the chest sounds indicated some abatement of the trouble, but on the ninth day the temperature rose again and ranged between 105 and 101 F. for the next five days, staying at 103 or thereabouts most of the time. The ears, nose and throat examined at this time were normal. December 12, the twelfth day of illness, the child seemed much worse. From this date rigidity increased, both sides being involved; there was some retraction of the head; contraction of the pupils, though not marked; a slight bulging of the fontanel and irregular breathing. The feet were edematous from contraction, and the bowel movements gave an offensive odor. The kidneys were acting normally. Mild convulsive attacks came on, lasting from twenty to thirty minutes. December 14 lumbar puncture was made. The fluid obtained was turbid, under pressure, and contained many polynuclear and few mononuclear cells. There were also small Gram-negative bacilli, both intra- and extracellular, which did not grow on plain media. The child failed rapidly and died that night.

Autopsy Report.—The autopsy was held one hour after death, and following is the anatomic diagnosis: acute purulent leptomeningitis (influenzal); acute bronchitis; bronchopneumonia; acute splenitis; cloudy swelling of the liver, heart and kidneys; acute swelling of the peribronchial lymph-glands; enlargement of tonsils; fatty liver; divergent strabismus.

The body was not emaciated. The pupils were equal and moderately dilated and the left eye diverged; no icterus. The anterior fontanel bulged slightly. In the peritoneal cavity were a few drops of clear fluid; in the pericardial cavity were a few cubic centimeters of slightly turbid fluid. The tonsils were dark red, slightly enlarged and the surfaces irregular. The nasal mucosa was reddened and in the upper part of the nasal cavity was a small amount of slightly purulent secretion.

The upper lobe of the left lung was normal. The lower lobe, especially in its posterior portion, was dark red and in places did not crepitate. On section regions were seen which were deep red in color and contained numerous small gray areas about 1 or more mm. across, from the centers of which exuded on pressure a small amount of pus. The tissue from these regions sank in water. No fibrin appeared on gross examination. From the larger bronchial tubes pus could be expressed.

The right lung in general resembled the left. The apex contained a small, slightly depressed region where crepitus was feeble and on section pus exuded from the smaller bronchi, which were surrounded by a narrow, light gray zone. The lower lobe was similar to the lower lobe of the left lung. The pericardium, heart, stomach, intestines, pancreas, adrenals and genito-urinary organs showed no noteworthy changes. The liver was fatty and the kidneys on section were dull red, soft, slightly swollen and the markings indistinct.

Brain and Spinal Cord.—There was an excess of distinctly turbid cerebrospinal fluid which appeared to be under increased pressure. Over the entire surface of the frontal lobes and in large patches over the other portions of the brain, especially the base, there was a thick, greenish-yellow, purulent exudate involving the pia-arachnoid. As a rule the exudate was more extensive in the regions of the blood-vessels and about the cranial nerves at the base. The vessels were intensely congested and the convolutions, especially over the frontal lobes, were very much flattened. No hemorrhages appeared. The dura was everywhere reddened, and at the base in places thick greenish pus adhered to its surface. The tympanic cavities showed no change.

The meninges of the spinal cord were intensely congested and a fibrino-purulent exudate was present throughout the canal.

Microscopic Examination.—Sections made of the cortex and meninges in the region of the larger vessels in the Sylvian fissure showed an extensive exudate in the pia. This consisted chiefly of polynuclear leukocytes, but in places mononuclear cells were common. Many of the former were disintegrated. The mononuclear cells had round or oval nuclei and a moderate amount of protoplasm. Plasma cells were rare. About the blood-vessels the exudate was abundant. Occasionally a few polynuclear and mononuclear cells were seen in the cortex near the surface and along the small blood-vessels penetrating the brain; no hemorrhages were found in the meninges or brain tissue. A similar exudate occurred in the cerebellum. The polynuclears were also abundant here and in places large phagocytic endothelial cells were common. In sections of the spinal cord were seen an extensive exudate in the meninges, especially enveloping the roots of the spinal nerves. Polynuclear leukocytes predominated but many mononuclear cells also occurred. There was intense congestion of the blood-vessels but no hemorrhages. Perivascular infiltration was beautifully seen about the small blood-vessels entering the cord from the pia. The central canal appeared unchanged.

In sections of the lung many polynuclear leukocytes were seen in the lumen of the bronchioles and the walls were intensely congested and infiltrated with round-cells and leukocytes. The alveoli in the region about the bronchioles usually contained exudate consisting of plasma-cells, leukocytes and, sometimes, fibrin. The tissue everywhere showed marked congestion and some edema. In the kidneys leukocytic casts were occasionally found in the tubules and in general the tubular epithelial cells were swollen and the nuclei stained indistinctly. A large amount of fat was seen everywhere in the liver. In the centers of the Malpighian bodies in the spleen areas of necrosis were often found. The myocardium, adrenals and thymus showed no significant changes.

Bacteriologic Report.—The cerebrospinal fluid was distinctly turbid but not bloody. In cover-glass smears were many polynuclear leukocytes and a few large mononuclear cells, and both within and without the leukocytes large numbers of very small bipolar Gram-negative bacilli were seen. Smears of the thick exudate showed the same bacilli and numerous leukocytes. Cultures of the fluid gave an abundant growth of typical *B. influenzæ*. On some plates were one or two colonies of *B. coli*, evidently a contamination, and about these the larger influenza colonies were grouped, showing characteristically their symbiotic property. Cultures of the heart's-blood gave on plates a pure growth of *B. influenzæ*. On some plates, purposely contaminated, numerous larger influenza colonies were grouped around the contaminating colonies. In smears and cultures made from the lung exudate *B. influenzæ* was found as the predominating organism. A moderate number of pneumococci were also present. In the pericardical fluid a few influenza bacilli were found in pure cultures. Examination of the peritoneal fluid and emulsions of the spleen and peribronchial lymph-glands for influenza bacilli gave negative results. A few colon bacilli were recovered from the peritoneal fluid. Careful search was made for influenza bacilli in the nasal secretion, but none was found. Many pus-cells occurred, and also a few staphylococci and many saprophytic organisms.

Serum from the heart's-blood obtained at the autopsy did not specifically agglutinate the bacilli from the spinal fluid, even in low dilutions. Animals were not highly susceptible. One c.c. of the cerebrospinal fluid injected immediately after the autopsy intraperitoneally into a guinea-pig was not fatal. The growth from two or three slants of pigeon-blood-agar given intraperitoneally was required to kill.

Case 4.—Infant girl, colored, aged 7 months, admitted to the Maternity Hospital Nursery, May 27, 1909. The child contracted a cold in the early part of December, 1909, which persisted, but was not severe. January 1, the temperature was 102 F. January 2, the temperature was recorded as normal, but January 3, it was 100 F. at 9 a. m. and the child looked ill. At 11 a. m. the temperature rose to 103 F. and a little later a convulsion occurred which lasted

for some time. Rigidity persisted, and, meningitis being suspected, the child was taken to the Presbyterian Hospital, where she rapidly grew worse, suffering several convulsions, and died during the night. Spinal puncture was made a few hours before death and a turbid fluid under pressure was obtained. It contained many polynuclear and few mononuclear cells; also many small Gram-negative bacilli, both intra- and extracellular, which did not grow on plain media.

Autopsy.—The autopsy was made six hours after death and the following anatomic diagnosis given: acute fibrino-purulent leptomeningitis; catarrhal bron-

Fig. 1.—Photograph of the hemorrhagic pseudomembranous exudate lining the dura in Case 5. In places it has been detached from the dura.

chitis; acute rhinitis; edema and congestion of the lungs; acute splenitis; fatty liver; cloudy swelling of the heart and kidneys.

The child was well nourished. Both eyes deviated strongly to the left; the pupils were equal but dilated; no discharge from the ears. The peritoneal cavity contained a few drops, and the pericardial cavity a few cubic centimeters, of clear fluid. The thymus, thyroid, heart, larynx and pharynx presented no significant changes. The nasal mucosa was covered by a thin layer of tenacious mucus and

Fig. 2.—Chart showing temperature curve in Case 6.

was distinctly reddened and edematous. No pus was present in the nasal cavities. The tonsils appeared normal. The upper and middle lobes of the right lung crepitated rather feebly and the lower lobe was nearly airless. The pleura was everywhere smooth and glistening and in some places dark purple in color. On section the tissue was very moist and bloody, but no regions of consolidation appeared. From the bronchial tubes a frothy non-purulent fluid exuded on pressure. The lobes of the left lung also crepitated everywhere, though very feebly in the portions of the lower lobe, in which the tissue was dark red in color and soggy. The cut surface was moist and bloody, and from the smaller bronchi, on pressure, exuded a mucinous, slightly turbid fluid. No areas suggesting pneumonic consolidation appeared. The peribronchial lymph-glands were enlarged and dark red in color, without central softening or other change. The liver showed slight

Fig. 3.—Photograph showing abscess formation in the left cerebrum in Case 6. Extensive softening of the cortex is also shown in the opposite hemisphere.

fatty change and the spleen was firm, swollen and had indistinct Malpighian bodies. The anterior fontanel tended to bulge slightly and the cerebrospinal fluid was increased in amount and was distinctly turbid but not bloody. Over the base and the surface of the brain, especially along the larger blood-vessels, was a thin, gray, fibrino-purulent exudate. The meninges were edematous and the convolutions were slightly flattened. The dura was deeply congested. In the meninges of the spinal cord a similar exudate was found. The tympanic cavities were both normal.

Microscopic Examination.—In sections through the cortex the exudate in the meninges was thin and composed almost entirely of polynuclear cells. In

places a few mononuclear cells appeared. The blood-vessels were intensely congested, but no hemorrhages were seen. Slight infiltration into the cortex of polynuclear cells occurred in places, especially along blood-vessels. Small bacilli were seen in the exudate. The exudate covering the cerebellum was more abundant, but was composed of similar cells. Extending along the spinal cord and enveloping the spinal roots was this same exudate, rich in polynuclear cells. The central canal was dilated and filled with exudate composed almost entirely of polynuclear cells. Little or no infiltration occurred in the surrounding tissue. In the lungs there was marked infiltration of round-cells, plasma-cells and leukocytes into the bronchial walls, with intense congestion of the blood-vessels. In the lumen were many polynuclear leukocytes. In the surrounding alveoli was a small amount of exudate containing some red cells and leukocytes. Marked edema occurred generally. Sections of the nasal mucosa showed marked infiltration, chiefly of round-cells into the mucosa, with congestion of the blood-vessels. Small areas of necrosis occurred in the centers of the Malpighian bodies in the spleen. The peribronchial lymph-glands, stomach, intestine, pancreas, adrenals, liver and kidneys showed no noteworthy changes.

Bacteriologic Report.—The cerebrospinal fluid, which contained a large number of polynuclear leukocytes and a few mononuclear cells in smear preparations, showed many small Gram-negative bacilli both within and without the leukocytes. In culture a pure growth of *B. influenzæ* was obtained from the exudate of the brain and the spinal cord. From the exudate of the left lung, which contained a considerable number of leukocytes, in culture were obtained many influenza colonies in symbiosis with the few pneumococcus colonies also present. Cultures of the heart's-blood also gave pure growth of the influenza bacillus. In the mucus scraped from the nasal mucosa a few colonies of this bacillus were obtained, and in addition many pneumococcus colonies. The pericardial and peritoneal fluids and the bile were sterile.

The homologous serum did not agglutinate the bacillus isolated from the heart's-blood, even in low dilutions. Growth from two pigeon-blood agar-slants introduced intravenously into a small rabbit produced no symptoms. The same amount injected intraperitoneally produced death in twenty-four hours and the bacillus was isolated pure from the peritoneal fluid and the heart's-blood.

CASE 5.—Infant, boy, aged 1 year. This case developed in St. Vincent's Infant Asylum. For some time there had been considerable "coryza" among the children, and several cases of bronchopneumonia, otitis media, etc., had developed. The nurses and attendants had been free from colds or "grip" infections. For several weeks previously the child suffered from bilateral otitis media and bowel disturbance, and became emaciated and anemic. Of late he was improving, when one week before death symptoms of bronchitis, fever and nasal discharge began, and later, evidence of bronchopneumonia. Five days before death meningeal symptoms appeared, manifested by rigidity of the back, neck and jaws, high fever, strabismus, moaning, etc.; a strong fetid odor from the nose and mouth was also noticed. Autopsy was made thirty hours after death.

Anatomic Diagnosis.—Acute purulent leptomeningitis; acute hemorrhagic pseudomembranous internal pachymeningitis; necrosis of nasal mucosa; bilateral purulent otitis media; bronchopneumonia; acute splenitis; parenchymatous degeneration of heart and kidneys; fatty liver; emaciation; strabismus; herpes labialis.

The child was emaciated. On the lower lip were small herpetic lesions. The anterior fontanel bulged slightly. The pupils were equal, moderately dilated and the left eye diverged. The sclerotics were pale and not icteric. In the pericardial cavity was about 20 c.c. of a clear, straw-colored fluid. Both lungs in the lower lobes showed small regions of pneumonic consolidation near the pleura on the posterior surface, which had a definite lobular distribution. In the bronchioles there was free pus. The upper lobes were normal. The lymph-glands about the hilus of the lungs were slightly enlarged. The liver was pale, rather soft and

in places light yellow areas were seen. The spleen was large, rather firm, brownish-red and the Malpighian bodies were indistinct. The kidneys were soft, large, and on section the tissue was swollen and dull red in color. The nasal mucosa was dark gray and covered by a thick, fetid, dirty, bloody membrane which extended downward into the pharynx and upward, where it could easily be traced, especially on the left side, to the cribriform plate. In the mouth, covering and adhering to the soft palate and also extending forward, was a bloody exudate appearing much like a blood-clot. The pharyngeal mucosa was red and covered with mucus; the larynx was covered with purulent mucus. The tonsils were not enlarged. In both tympanic cavities was a dirty looking pus but there was no evidence of invasion of the cranial cavity from these points. On opening the skull about a pint of bloody serous fluid escaped from the subarachnoid space. Lining the entire inner surface of the dura and slightly adherent to it was a definite fibrinous pseudomembrane, dark red in color, and 1 to 2 mm. thick (Fig. 1). This was not adherent to the pia. In the pia was an abundant purulent exudate which was bright red in color and distributed in patches, especially along the larger blood-vessels. At the base and beneath the frontal lobes the exudate was very abundant, and in this the olfactory lobes were imbedded. The cerebrospinal fluid was milky in appearance and had only the slightest tinge of blood. The purulent exudate extended downward into the meninges of the cord, but there it was not abundant. The bloody fibrinous pseudomembrane was also visible about the cord and extended to the cauda. The vessels in the meninges everywhere were deeply congested.

Microscopic Examination.—In sections of the cortex and pial exudate was seen an extensive infiltration into the meninges, consisting largely of polynuclear cells. There were a few mononuclear and plasma cells and here and there were considerable numbers of large endothelial-like cells often containing englobed leukocytes. In many of the small blood-vessels the lumen was filled with leukocytes, and occasionally the lining endothelial cells appeared swollen and cuboidal in shape. The walls were usually infiltrated with cells and thrombi could be seen in the vessels. The cellular infiltration into the cortex was very slight, there being only an occasional leukocyte seen, except along the small vessels penetrating the cortex from the pia where there could be seen, as a rule, a definite though not an extensive infiltration of round and polynuclear cells. Small hemorrhages occurred in this exudate. Distinct from this pial exudate was the extensive pseudo membranous exudate in contact with the inner surface of the dura. In sections the exudate was seen to be in intimate contact with the fibrous layers and was made up of an organizing layer containing round and elongated cells and some leukocytes. Fibrin was not abundant and in some places red cells were common. The dura itself was little changed. Sections of the cord made through the cervical portion and the cauda showed an extensive exudate, especially abundant about the nerve-roots, and there could also be seen in the cervical sections a layer lining the dura made up of red blood-cells, fibrin and leukocytes, which evidently corresponded to the cranial subdural exudate. This was also evident in sections through the cauda. The central canal contained an exudate consisting of leukocytes and round-cells.

In sections of the lung was seen a leukocytic exudate in the alveoli, especially those adjacent to the bronchioles. The latter were filled with leukocytes, and the walls were congested and infiltrated with cells, chiefly polynuclear and plasma-cells. Fibrin could be seen, but it was not abundant. The pleura was congested and in places covered by a delicate, fibrinous, cellular exudate. In the spleen were seen numerous areas of necrosis in which were round and lymphoid cells, and an eosin-staining homogeneous intercellular substance. These areas were definitely circumscribed and were located within or near the margin of the Malpighian corpuscles; no hemorrhages. Small hemorrhages occurred in the adrenal gland. The liver, pancreas, thyroid, intestinal mucosa, kidney, thymus and myocardium were not altered.

The cerebrospinal fluid, obtained at the foramen magnum, was milky in appearance and abundant. Cells were numerous and consisted of three varieties in the following proportions: Polynuclears, 66.4 per cent.; mononuclears, 30 per cent.; large endothelial cells, 3.6 per cent.

Bacteriology: In smears of the cerebrospinal fluid and the meningeal exudate were myriads of small Gram-negative bacilli both within and without the numerous polynuclear cells present. Cultures consisted of a nearly pure growth of *B. influenzæ;* a few large colonies, evidently of saprophytic bacilli, appeared also, and about them the influenza colonies were clustered. Anaerobic cultures of the exudate gave no significant organisms. In the middle ear were many streptococci and profusely growing saprophytes; no influenza bacilli. The heart's-blood, material from nose and other parts, contained such enormous numbers of saprophytic bacteria, probably post-mortem invaders, that the examination was unsatisfactory. No influenza bacilli were obtained in cultures of these fluids, though in smears Gram-negative minute bacilli suggestive of them were seen.

The growth from two small pigeon-blood-agar slants of the bacillus from the cerebrospinal fluid injected intraperitoneally killed a guinea-pig in eighteen hours and the organism was recovered from the heart's-blood and peritoneal exudate of the animal. A similar amount injected subcutaneously in a guinea-pig produced no symptoms. The bacilli were not specifically agglutinated by the homologous serum, even in low dilutions.

CASE 6.—Infant, girl, aged 10 months. One month before death the child caught cold and had some fever. Later she lost strength and weight, slept much of the time, and suffered from regurgitation of food. Ten days before death the child entered the Presbyterian Hospital, having marked rigidity of the neck and limbs; was in a stupor and unable to retain food. The anterior fontanel was bulging and eye symptoms were marked. Harsh breathing was present over the right upper lobe but there were no definite areas of dulness. Spinal punctures were made several times and a turbid fluid under pressure, containing many polynuclear leukocytes (90 per cent.) and Gram-negative small bacilli, was obtained. There was no growth in cultures on plain media. The temperature ranged from 100 F. to 104 F., as a rule, but on the day before death it dropped to 98 F., then suddenly rose to 105.8 F. (Fig. 2). The pulse was variable, usually ranging from 130 to 160 and the respirations ranged from 20 to 60. The leukocyte count was 21,050 and hemoglobin 80 per cent.

Autopsy.—Autopsy was held four hours after death. Anatomic diagnosis: acute fibrino-purulent leptomeningitis (influenzal); acute softening of right cerebral cortex; abscess in left cerebrum; internal hydrocephalus; bronchopneumonia; acute purulent bronchitis; fibrinous pleuritis; acute rhinitis; sub-pleural hemorrhages in right lung; petechial hemorrhages in skin; acute splenitis; septic infarcts in the spleen; fatty liver; acute degeneration of the kidneys and myocardium; localized fibrinous peritonitis; external strabismus; rachitis.

The anterior fontanel bulged slightly. On the abdomen, especially in the regions of the umbilicus and on the back were numerous small petechial hemorrhages, pin-point in size. There was no free fluid in the peritoneal cavity, but on the surface of the spleen and on the adjacent peritoneum were small gray flakes of fibrin. There was distinct enlargement of the juncture of the costal cartilages and the ribs. The tracheal mucosa was covered with a thin layer of grayish mucus which at the bifurcation was slightly purulent. In the lower lobes of both lungs, chiefly in the posterior portions, were consolidated areas showing a lobular distribution, and on pressure pus exuded in abundance from the bronchial tubes. Small pneumonic areas also existed in the upper lobes. The cut surface through the consolidated areas was dull gray, and as a rule mottled with red areas. In the pleura of the right lower lobe were small hemorrhages and over the consolidated portions the pleura was covered by a thin layer of fibrin. The peribronchial lymph-glands were large, soft and pink; no necrosis. The heart, thyroids and thymus were unchanged.

The spleen was large, firm and purplish-red in color and portions of the capsule were covered by a thin layer of grayish-yellow fibrin. The cut surface was red and the Malpighian bodies were small and indistinct. Along the anterior margin under the capsule were a number of small, yellow, soft areas 2 or 3 mm. across, which involved the substance of the spleen to a depth of 2 mm. or more. These areas appeared necrotic, but no pus exuded on section. The liver was soft, yellowish-brown in color and the lobules were very indistinct. The kidneys were soft, markings indistinct, and on section the cortex appeared pale and swollen. The remaining viscera showed no noteworthy changes.

On opening the cranial cavity a large amount of turbid cerebrospinal fluid was encountered. The brain was very soft and everywhere there was an abundant greenish-yellow, highly purulent exudate. This was especially abundant along the larger vessels and along the base. Over the hemispheres it was arranged in patches or islands surrounded by relatively clear meninges. The convolutions were flattened, especially in the frontal lobes and at the base. The brain, on section, showed an extensive area of softening involving the right cortex from the median fissure to the Sylvian fissure, chiefly in the Rolandic area. On the opposite side an abscess (Fig. 3) containing a large amount of greenish-yellow pus was found just below the surface and extending down to and into the lateral ventricle. There was no definite wall, the tissue at the margin being soft and necrotic. No definite hemorrhages occurred. Distinct dilatation of the ventricles was present especially evident in the fourth ventricle. The exudate extended throughout the spinal canal, but there it was less abundant than in the cranial cavity. The meninges were intensely congested everywhere. The cranial dura was red in places and here and there thick green pus adhered to its inner surface. The tympanic cavities appeared normal. There was a small amount of gray, purulent mucus in the nasal cavity, and the mucosa was smooth, but slightly reddened, and was covered by a thin layer of mucus; no necrosis.

Microscopic Examination.—In the lungs the bronchioles showed intense inflammatory changes, consisting of degeneration of the epithelium, and congestion and marked infiltration of plasma-cells in the submucosa. Polynuclears were abundant in the lumen but rare in the submucosa. The alveoli contained many polynuclear leukocytes, and in places a small amount of fibrin. In sections through the softened portions of the brain could be seen many bacterial emboli in the small blood-vessels. The bacteria resembled influenza bacilli and were largely confined to the vessels. Very slight infiltration occurred in the surrounding tissue, which stained poorly. No definite abscess wall was visible. The meninges showed intense congestion and infiltration, chiefly with polynuclear cells.

Bacteriology.—In the purulent exudate from the surface of the brain and in the cerebrospinal fluid were myriads of minute Gram-negative bacilli which on culture proved to be *B. influenzæ*. They also occurred in large numbers in the bronchial pus, but were not isolated in culture from the other body fluids, though in smears of the nasal exudate numerous small Gram-negative bacilli were seen. In the meningeal and bronchial pus there were also a few streptococcus colonies on the blood-plates and this organism was also found pure in the heart's-blood and pericardial fluid and mixed with saprophytic bacilli in the nasal cavity.

One c.c. of the greenish pus from the cortex was injected subcutaneously into a guinea-pig. On the following day the animal appeared inactive and later lost some weight; after a few days it had entirely recovered. A second pig was injected with one pigeon-blood agar-slant culture intraperitoneally. Death followed in twenty-four hours, there being edema of the abdominal wall and marked peritonitis. The bacillus was recovered from the heart's blood and the peritoneal fluid.

Agglutination experiments using the homologous serum were negative.

CASE 7.—Infant boy aged six months. Forceps delivery at 8 months; child in good health until the present illness. Feb. 17, 1910, the child was taken sick with vomiting and fever (102.5 F.), and the mother noticed a peculiar

quivering of the chin. During the night he moaned almost constantly and the next morning (February 18) appeared sick, pale and waxy. In the afternoon several convulsions occurred. At this time the child was unconscious, the neck was rigid, the pupils did not react to light and there were twitchings of the left side of the face, angle of mouth and the left hand and foot; both limbs on the left side were rigid and Kernig's sign was absent. There was slight dulness over the right lung posteriorly. Spinal puncture gave an abundant turbid fluid, which contained a large number of cells, nearly all of which were polynuclear leukocytes. There were also present many very small Gram-negative bacilli, mostly extracellular, but some definitely intracellular. They were distinctly polar-staining, and occasionally thread-like forms appeared. They failed to grow on plain media. Morphologically these bacilli were typical *B. influenzæ*. Unfortunately the cultural properties were not studied, as blood media were not inoculated. Two injections of 25 c.c. each of Flexner's serum were given without result. The child gradually became worse and died February 20, three days after the initial symptoms began. No autopsy.

GENERAL CONSIDERATIONS

These seven cases of influenzal meningitis occurred in Chicago in the course of little over a year, all resulting fatally, and in duration varying from three to fourteen days. All were infants, the oldest being 13 months and the youngest (twins) 5 days old. A definite history of colds preceding the meningeal trouble, as a rule, several weeks, was obtained in four cases. The occurrence of the disease in the twins, beginning simultaneously, is suggestive of a common source of infection, but in this instance it could not be determined. Cases 3 and 4 came from a small institution[10] for children in which an epidemic of "colds" had existed for several weeks. The children were all in intimate contact constantly with each other. In Case 4 the patient developed the disease about four weeks after the child in Case 3 was taken ill, or about two weeks after her death. A few days after the death of Patient 4, and while a number of the children were suffering from colds, though not severely ill, swabs were taken from the noses and throats of all the children (twelve cases) and examined in smear and by pigeon-blood agar-plates for influenza bacilli. The results were negative in all cases. *Streptococcus pyogenes* was numerous and generally was the predominating organism in all cases. Staphylococci and pneumococci were also common. Case 5 also developed in an institution for children at a time when many cases of "colds," and especially bronchopneumonia were occurring there. The children did not come from the poorer parts of the city, and, excepting the association of Cases 1 and 2 and Cases 3 and 4, no relation could be ascertained. Cases 1 and 2 developed in October, 1908; the others occurred in the winter months of 1909-1910, during which period a general influenza epidemic was not raging.

10. This institution is conducted by Dr. Effa Davis, to whom I am indebted for the opportunity to examine the cases bacteriologically.

As a rule the onset in these cases was indefinite and the exact time when the meningeal trouble began could not always be determined. Eye symptoms were usually present and in all cases rigidity of the back and the limbs and retraction of the head were marked. Definite convulsions occurred in five cases. Other early symptoms were cough, harsh breath-sounds or definite signs of pneumonia, bowel disturbances and restlessness. Bulging of the fontanel was evident in all cases and herpes labialis was present in one case. Small petechial hemorrhages in the skin occurred in Case 6 a short time before death. The temperature generally was variable, ranging from normal to 105 F. or higher, and subject to sudden change (Fig. 2). The pulse was irregular but usually rapid (130-160). The period of incubation cannot be over five days, since the twins became ill on the fifth day after birth.

Lumbar puncture was made in four cases and in all there was obtained a turbid fluid, under high pressure, in which were many leukocytes, the polynuclear cells always predominating. Differential counts gave from 60 to 80 per cent. polynuclear cells, the remainder being chiefly small mononuclear cells. Endothelial cells were also commonly found. Red cells were not found, or occurred in small numbers and the fibrin was scant.

Five of the seven cases were examined post mortem. An abundant, highly purulent, greenish-yellow leptomeningeal exudate was found in four; in the remaining child (Case 4), which died on the third day, the exudate was less profuse and limited chiefly to the base and the vessels in the Sylvian fissure. Generally the exudate was very abundant at the base and about the frontal lobes and in these regions marked compression of the convolutions occurred. Often the exudate over the cortex was distributed in large patches and usually was much more abundant along the blood-vessels. In one case (Case 5), delicately attached to the dura, was an extensive hemorrhagic exudate which, after hardening, closely simulated a definite membrane. This was entirely independent of the purulent pial exudate, from which it could readily be separated. On microscopic examination this exudate was found to consist of red-cells and layers of fibrin, together with an infiltration of leukocytes and fibroblasts. In sections of the spinal cord, even at the cauda, this membrane was observed on the inner surface of the dura and independent of the more purulent exudate involving the pia-arachnoid. Exudates of this type have not been reported in influenzal infections of the meninges, though similar changes have been described in connection with meningococcus infections. In all cases the dura was red and congested and usually some of the greenish, thick pus adhered at the base after removing the brain. In Case 6 a very extensive softening containing thick greenish-yellow pus in which were bacilli in abundance formed under the cortex

and penetrated the lateral ventricle. This is the first case of this disease in which a cerebral abscess has been noted. On the opposite side of the brain was extensive softening of the cortex, but no definite abscess formation.

In none of the cases did hemorrhage into the brain substance occur. Acute hydrocephalus was marked in Case 6, a condition noticed by others in influenzal meningitis, and also not a rare occurrence in other forms of meningitis.

The spinal cord was removed in four cases and in general the exudate here was less in amount than in the cranial cavity. Usually it was more abundant on the posterior surface and was profuse in the pia-arachnoid and about the nerve-roots. Often the infiltration penetrated the substance of the cord, especially along the blood-vessels, and could be traced well into the gray matter. Pus was seen in the central canal of the cord in two cases (Cases 4 and 5).

Histologically the exudate was extremely rich in cells, and fibrin was absent or present in traces, so far as one could tell from the formalin-fixed preparations. The cells were of three types, namely, polynuclears, mononuclears and large endothelial-like cells. In certain areas the exudate was composed almost exclusively of polynuclears; in other parts mononuclears and the endothelial cells were common. The latter often had from one to three polynuclear or mononuclear cells included in their protoplasm. These cells appeared to be the desquamated endothelial cells which line the arachnoid spaces, which have been noted in meningococcic meningitis, especially by Councilman. Sections stained for influenza bacilli revealed the organisms in the exudate. Small hemorrhages were sometimes seen in the exudate and the blood-vessels at times were thrombosed and the walls infiltrated with cells. Always the exudate followed the pia into the deepest sulci and often extended for a short distance along the vessels into the cortex. The infiltration of the cortex, however, was generally not extensive and excepting the softened areas and abscess in Case 6 it was limited to the occurrence of a few polynuclear and plasma cells near the surface.

In one case bilateral purulent otitis media had been present for several weeks. Acute rhinitis was found in three cases, one (Case 5) showing extensive necrosis of the entire nasal mucosa, involving the cribriform plate and extending downward into the pharynx. The tonsils were slightly enlarged in two cases. Acute bronchitis was present in four and bronchopneumonia in three cases. The pneumonic consolidation, as a rule, involved the posterior portion of the lungs and was more extensive in the lower lobes. It was distinctly of the lobular type and the infiltration about the bronchioles in the peribronchial lymph-channels was characterized by the presence of large numbers of plasma cells. As a rule

few polynuclear cells appeared here. Fibrin was scant, though in places it was definitely visible. The exudate in the bronchial tubes and in the alveoli contained chiefly polynuclear and desquamated epithelial cells.

In no instance was there effusion into the pleural cavities, but in three cases, in which bronchopneumonia existed, the pleural surface over the involved regions was granular and lusterless. In Case 6 there was a marked though not extensive fibrinous layer covering the pleura and beneath were numerous small but definite hemorrhages. In this connection may be mentioned the hemorrhages on the surface of the thymus in Case 1, and the petechial hemorrhages in the skin in Case 6. In all cases the liver presented evidence of fatty change. Icterus was not noted.

It was common to find a small amount of slightly turbid fluid in the peritoneal cavity. In Case 1, influenza bacilli were obtained in considerable numbers from this fluid but there was no macroscopic evidence of peritonitis. In Case 6 on the spleen and regional peritoneum was a definite gray, fibrinous exudate originating and extending from the infarcted areas in the spleen. The adrenals showed no noteworthy change in any case. Generally, acute degeneration of the various viscera was evident.

The various fluids of the body collected at autopsy were studied bacteriologically in smear preparations and on pigeon-blood agar-plates. The influenza bacillus was isolated in practically pure culture from the meningeal exudate and cerebrospinal fluid in all post-mortem cases. They were present usually in enormous numbers, as shown by the smear preparations, and were always both within and without the polynuclear cells. In two cases (3 and 4) they were found pure in the heart's-blood in large numbers. In both these cases the autopsy was held while the body was still warm; consequently there can be no doubt that the bacilli were present in the circulating blood before death and might have been isolated by blood-cultures, had such cultures been made. In one case the bacilli were found in the peritoneal fluid and once in the pericardial fluid. In three cases they occurred mixed with streptococci in the bronchial secretions, and once they were grown from the surface of the nasal mucosa. On account of the difficulty with which this organism sometimes grows it is possible that its distribution was more general than the positive cultures indicated. In smears from the nose Gram-negative minute bacilli were found in two cases, which were not recovered on the plates. In Case 5 in which there could be no doubt that the infection invaded the cranial cavity through the cribriform plate from the nasal cavity, no influenza bacilli were recovered from the nasal exudate, probably on account of the presence of large numbers of other organisms. In Case 6 a terminal streptococcus infection occurred, these organisms being found in the heart's-blood, pericardial fluid, nasal exudate and bronchial pus. A few were also found in the meningeal exudate, but in insignificant num-

bers compared with the influenza bacilli, myriads of which, in symbiosis, were crowded around the streptococcus colonies. That the streptococcus was a terminal infection is evidenced by the fact that this organism was not found in culture of the spinal fluid obtained by lumbar puncture before death.

The atrium of infection was not certain in all cases. In Case 5 the infection could be traced directly from the nasal cavity through the necrotic cribriform plate. In Case 4 the bacilli were found in large numbers on the inflamed nasal mucosa, and in Cases 3 and 6 the infection probably originated in the upper respiratory passages. Four of the cases had bronchitis or pneumonia, from which lesions the bacilli were isolated. From the clinical data, however, one cannot be certain whether or not these lesions antedated the meningitis. In Case 1 gastro-enteritis was present at autopsy, symptoms of which appeared at the onset. The massive meningeal exudate under the frontal lobes and at the base of the brain in all cases points rather strongly to a nasal origin, and the fact that generally these cases had been troubled with infections of the upper respiratory tract would seem to substantiate this idea.

Morphologically and biologically the influenza bacilli isolated in these cases were in no way different from bacilli commonly found in sputum in various infectious diseases. They were very minute, Gram-negative, distinctly bipolar when stained, and susceptible to phagocytosis. In smears of the meningeal pus one occasionally saw some tendency to form threads, this being most marked in Case 7. In cultures, as a rule, this tendency was greater, not infrequently long and curved thread-forms being common. In the culture from Case 6 this was especially noted, and at times growths were obtained which were made up largely of long threads resembling a leptothrix. The colonies of the various strains presented the typical dew-drop appearance, were not hemolytic, and grew only in hemoglobin media, with a preference for pigeon-blood-agar.

The property of symbiosis was marked in all strains. Attention should be directed to this very important characteristic, which serves to distinguish this organism from other closely related bacilli. Advantage was taken of this property in the examination of the various fluids by purposely contaminating the plates or media with other germs. In some instances positive influenza cultures were thus obtained about the foreign colonies when growth was not evident in the uncontaminated cultures. It is therefore advisable at times to thus purposely contaminate the media, using of course proper controls, when searching for this bacillus in spinal fluid, blood, and other fluids.

Serum was obtained from the heart's-blood in four cases and its agglutinating power tested, using the homologous bacilli, and also bacilli

from other cases. The results were negative. Both macroscopic and microscopic methods were used.

The bacilli isolated post mortem were all tested on guinea-pigs or rabbits with the following results: injected into the peritoneum of guinea-pigs, growth from two small agar-slants caused death in twenty-four hours. Subcutaneously this amount was not sufficient to cause death. Several drops of thick pus from the meninges intraperitoneally in guinea-pigs was not sufficient to cause death. Compared with bacilli from sputum of other cases they appear to have about the same degree of virulence. All strains were quite similar in their pathogenicity and could not be called highly virulent for the animals tested.[11]

I am indebted to Dr. F. S. Churchill for the clinical reports in Cases 1, 2 and 7, and to Dr. Effa Davis for the clinical records of Cases 3 and 4. Case 5 developed in St. Vincent's Orphan Home in the service of Dr. Baxter, and in Case 6 the patient entered the Presbyterian Hospital in the service of Dr. Cotton.

11. Cohen (see note 3) found that the bacilli from his cases were highly virulent for animals, tending to produce a rapid and fatal septicemia. On this fact, and also on certain facts obtained with the conglutination reaction, he attempted to differentiate these meningitic bacilli from the true Pfeiffer's bacillus. It is probable that he was dealing merely with a more highly virulent influenza bacillus.

OBSERVATIONS ON THE TREATMENT OF CHRONIC INFANTILE PARALYSIS

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The triumphant event in the study of chronic infantile paralysis is the change in the minds of the profession toward a more favorable prognosis. Whereas only a decade ago the accepted verdict was that "muscles which do not recover in the first weeks or months usually remain paralyzed for a whole life time" (Strümpell), now the belief is that "treatment faithfully and persistently continued is frequently rewarded by the return of power and usefulness in the atrophied and helpless limb" (Young).

Coupled with this change is the growing confidence in the simpler forms of treatment for this disease. For instance, it has but recently dawned on orthopedists that in tendon transplantation the benefits derived were due to the persistency of the after-treatment rather than to the substitution of a healthy tendon for a degenerated one. In the Hospital for Deformities and Joint Diseases of the City of New York, where approximately 1,100 cases of chronic infantile paralysis were treated within the last four years, the methods used were as follows:

Scarcely any tendon transference, arthrodesis, tenodesis, or nerve-grafting were done, while operations were limited only to the correction of paralytic deformities. Braces were avoided as much as possible, because of their tendency to lull the parents into the false belief that the child was wearing something which would cure him, and thus tend to make them neglect the treatment. Hand massage, the interrupted galvanic, the faradic and the sinusoidal currents were used. Practically all cases, not only those in the recessional stage, in which improvement is physiologic, but those also in which the paralytic attack was of over a year's duration, improved under this treatment. This is especially so in those cases in which previous treatment was neglected or imperfectly carried out.

EFFECT OF MASSAGE IN INFANTILE PARALYSIS

Sometimes a child suffering from this disease cannot contract a muscle or a group of muscles, not because they are paralyzed, but because they are inflamed. When this is the case the child winces or cries with pain when the muscles are massaged, while palpation of these muscles elicits tenderness. This tenderness is caused by the hyperstretching of the paralytic muscles, which injures the contractile element and produces

a myitis or an actual neuritis. Massage helps to overcome the inflammation and voluntary motion is possible.

Straining the ligaments of the joints is common in infantile paralysis, because in urging the child to walk, his weakness produces abrupt movements which cause strain. Paretic muscles are also incapable of much exertion. In exercising these patients we are apt to overwork them, which causes stiffness of the muscles the next day, so that often patients cannot do their exercises as well as they did at the previous treatment. Massage helps to relieve the sensitiveness of the muscles and ligaments, which is caused by the above strain and fatigue.

The hardest part of the exercises occurs at the beginning when the child has to overcome the locking of the muscles. This locking of the muscles is produced by the hyperstretching of the paralytic group and the contracting of their opponents. Massage stimulates the contractile element of the stretched muscles and tends to relax the spastic opponents. It also raises the temperature of the muscles. This raised temperature, usually from 1 to 5 degrees Fahrenheit, renders the muscles electrically susceptible, i. e., it takes a smaller amperage to cause contraction of paretic muscles after massage than before. The importance of this phenomenon from a therapeutic standpoint is self-evident.

The belief that massage builds up atrophied muscles I find to be incorrect. In the Lucus-Championière method for the treatment of fractures, in which the limb is thoroughly massaged daily, massage diminishes but does not prevent the atrophy of muscles. Nor does massage and electricity prevent atrophy of inactive muscles. I have tried this a number of times on limbs that were held by posterior splints for inflamed joints. Despite the daily use of massage and the interrupted current, flabbiness of the muscles appeared in a short time. If, therefore, massage or the use of massage and electricity do not prevent the atrophy of healthy but inactive muscles, these agents certainly cannot "build up" atrophied and partly degenerated muscles, such as exist in chronic infantile paralysis.

Atrophy seems to be the result of the law of supply and demand of the organism, which is, that increased function of tissue is followed by the increased size and strength of the tissue; diminished function by atrophy, and useless tissue by degeneration. The lesion in chronic infantile paralysis is a destruction of motor cells in the spinal cord, while the part of the cord affected is shrunken and sclerotic. Improvement in the chronic stage is not due to the regeneration of motor cells in the spinal cord. The pathologic law that dead organic cells never regenerate is fixed. Improvement is due to the physiologic law that cells increase in size and strength with function, and that sometimes a cell takes over to itself the function of the destroyed neighboring cell. This must be true. How else can we explain the improvement that takes place in the chronic

stage of this disease and the fact that many children gradually outgrow their trouble?

In order to understand the *modus operandi* of the treatment in the chronic stage of this disease, we must first glance at the structures that are involved in a voluntary muscular contraction. They are, the motor cells in the spinal cord, the spinal nerves, the muscles, the conducting tracts, the motor centers in the brain, and the will power. In chronic infantile paralysis there is a break in this psycho-neuro-muscular cycle at the motor cells in the anterior cornu of the gray matter of the spinal cord. Atrophy and degeneration in chronic infantile paralysis is not only limited to the muscles, but also affects the nerves, the conducting tracts and the motor cells in the brain centers dominating the affected muscles, and the will power to concentrate on these brain centers becomes weakened from disuse caused by the break in the cycle.

Since the contractile element of the muscles is often injured or destroyed by the hyperstretching of the paralyzed muscles or by atrophy and degeneration, it is obvious that the care of the muscles themselves is imperative in this disease. Massage and electricity exercise the muscles, but the exercise produced by these agents is of a passive variety (an exercise of muscles without the exercise of the other structures of the cycle), and clinically we know that the benefit of passive exercise is slight. Permanent benefit is only derived from the simultaneous and coordinated exercises of all the elements of the cycle. This is only possible during voluntary muscular contraction, because in this wise the will power and the atrophic brain cells are exercised and by reciprocal action the motor cells in the spinal cord are developed and the muscles strengthened. And so, at bottom, it is the exercise of the will power that causes improvement in chronic infantile paralysis, by developing the gray matter in the brain and cord.

The dominant effect of massage is suggestion. The suggestion of massage in chronic infantile paralysis differs, however, from the psychic effect that massage has on the adult patient in other diseases. In the adult patient massage makes him feel that he is being "benefited," an element in massage long recognized, which explains its popularity in the treatment of nervous diseases. In chronic infantile paralysis in children, however, massage suggests focusing their will-power on the motor brain centers of the affected muscles and stimulating them into action. Suggestion itself, however, may not produce the desired effect or may even produce an opposite effect, which is true oftentimes of suggestion in general as, for instance, when a physician suggests or tells a neurasthenic that he is free from organic diseases and that he will get well, the patient becomes convinced that the opposite is true. Resistance to suggestion or command is often observed in the beginning of treatment of children with

chronic infantile paralysis. The strange surroundings of the dispensary or office, the manipulations, etc., frighten the child and arouse its antagonism, so that the child persists in contracting the muscles under massage and suggestion, or command to contract the paretic muscles is followed either by no response at all or only by desultory and superficial contraction.

The masseuse, however, towers over the child, grasps the limb with one hand and with the other executes movements on the body of the child which are centripetal or circular and which induce a tingling and a thrilling sensation. These movements are monotonous and are made in front of the child and resemble the passes of a hypnotist. I have seen children who when first massaged were unhappy and cried, but later become used to it and lie during the treatment completely relaxed with flushed faces and dreamy looks, a condition resembling the prehypnotic state in which the mind becomes susceptible to impressions. These various manipulations (rubbing, kneading, striking, etc.), performed during that period are suggestions to the child to contract the involved muscles. These suggestions repeated so frequently accumulate into a hypnosis which arouses and concentrates the child's will power on muscular contraction.

We see this often, in fact, when children who at the beginning of the treatment respond feebly to the command to contract their muscles, later begin to focus their energy to such an extent that their faces are flushed from the exertion. These extreme efforts can hardly be explained by the theory of the child's own initiative, but are rather prompted by a hypnosis which resulted from the movements of the masseuse.

PASSIVE MOTION

In passive motion the masseuse relaxes the stretched muscles and stretches the contracted ones. This is temporary, however, as the muscles slip back to their former position as soon as the hand of the operator is removed. During passive motion no muscular contraction takes place, and the effect, therefore, of these movements on the muscles themselves are practically nil. Its value is chiefly due to the fact that during the relaxation of the stretched muscles and the stretching of the contracted muscles such movements are suggested to the child.

ELECTRICITY

"Except as a matter of exercise, electricity is practically useless" (Sachs). The interrupted currents exercise the muscles and hinder the atrophy and degeneration which progress in the muscles. The exercise, however, induced by the currents is of a passive variety, since it affects the muscles alone, and the benefit of such exercise is slight. We see

cases in which a group of muscles have regained their power (as shown by their response to the faradic current), and still the child is unable to contract them. This can be accounted for by the child either forgetting how to contract the muscles during the period of their inactivity, or by his will-power to concentrate on these brain centers becoming weak from disuse. I believe that the chief value of the interrupted currents is not due to their local effect on the muscles, but is due to the impulses of the muscular contractions that are conveyed and registered on the child's brain. These impulses are object lessons to the child which imperatively suggest imitation of the movements.

CONCLUSIONS

The benefits of massage, electricity and passive motion are not due to the local effect of these agents on the muscles. In chronic infantile paralysis the affected muscles are unbalanced, atrophied and partly degenerated, are subnormal in temperature and have subjective symptoms of weakness, stiffness in exercise, and often of pain. The above agents, especially massage, relieve the pain by their counter-irritating effect, and the stiffness by their antispasmotic action, and temporarily raise the temperature and relieve the weakness by exciting the circulation and stimulating the contractile element in the paretic muscles. These effects help the patient to bring the muscles under the control of the will-power and facilitate their exercise. The chief value of these agents, however, is due to their reflex mental action, consisting of suggestions, of impulses of muscular movements which are conveyed to the brain, and which the child instinctively imitates, and the building up of an hypnosis which arouses the mental energy of the patient into a concentrated effort during the muscular contractions.

That this is true is proved by observations in the gymnasium. A bright child, for instance, a type generally susceptible to impression, makes greater progress during the treatment than the stupid child, a type not susceptible to suggestion. No matter how much local treatment the latter receives, he remains unresponsive and makes little progress. It is also proved by cases in which physicians have given a great deal of local treatment, together with a bad prognosis, and the patient has made but little progress during that time. Finally, perhaps, an intelligent parent or nurse may have applied herself with energy to the treatment of the child and produced remarkable results in a short time. Instances of that kind are not at all rare, and reports of such occurrence have of late found their way into the lay press.

The prime factor in these "miracles" has been the enthusiasm for work aroused in the child. In most of them very little local treatment was used, and it was mainly limited to massage. The form of massage

employed consisted generally of upward and downward strokes, the effect of which was to stimulate the nerve endings and draw the blood temporarily to the surface. Such massage, which is conspicuous for its flagrant disregard of all the principles of scientific massage, has little effect on the muscles themselves. Its reflex mental effect on the patient, however, is tremendous. It is practically the fetish which creates the enthusiasm. It is the carrier of the hypnotic impulses that arouse the will power to concentrate to the utmost during the muscular contractions, and which leads to the building-up of the mental and motor brain-cells.

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A STUDY OF BLOOD-PRESSURE IN NORMAL CHILDREN

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It was 100 years after Harvey's discovery of the circulation of the blood that Hales demonstrated blood-pressure (1733), but it was a century later before physiologic experiments gave any reliable results. Ludwig[1] in 1847 was the first to obtain a blood-pressure tracing, by means of a recording manometer directly connected with an open artery. These experiments quickly led to the introduction of clinical methods. V. Basch in 1882 constructed the tonometer, the perlotte of which could be placed over any artery. Roy and Adami[2] in 1890 constructed the first instrument based on direct compression of the artery—a flexible rubber bag containing water to exert the pressure and a mercurial manometer for a recorder. In 1896 Riva Rocca and Leonard Hill independently substituted air for water in the bag for compression and, although a number of other instruments have since been invented, the Riva Rocca model is the one which has proved most practical for general use.

V. Basch[3] as early as 1894 advised sphygmomanometry in children, and took the pressure with his tonometer in sixty-eight children in Monti's clinic in Vienna. In 1893 Friedman[4] took the blood-pressure of a number of children in Heubner's clinic, but drew no definite conclusion. The first important work was done by Oppenheimer and Bauchwitz[5] in 1905 and was followed by Eminet's[6] in 1907 and Seiler's[7] and Wolfensohn's[8] in 1910.

Age is the factor on which the standard of blood-pressure has always been based, but the normal limits have varied greatly according to different observers. In infants the pressure ranged from 75 to 90 mm.; in children over 2 years from 90 to 115 mm.; in young adults from 115 to

1. Janeway: The Clinical Study of Blood-Pressure, 1904.
2. Oliver, G.: Studies in Blood Pressure, 1908.
3. Von Basch: Ueber Pulse Fuehlen, Pulse Schreiben, und Pulse Messen, Arch. f. Kinderh., v, 7.
4. Friedman: Jahrb. f. Kinderh., lxiii-lxxxv.
5. Oppenheimer and Bauchwitz: Ueber den Blutdruck bei gesunder Kinder, Arch. f. Kinderh., 1905, xlii.
6. Eminet: Sphygmographie und Tonometrie bei gesunder Kinder, Arch. f. Kinderh., 1907, xlvi.
7. F. Seiler: Ueber den Blutdruck im Kindesalter. Cor.-Bl. f. Schweiz. Aerzte, May 10, 1910.
8. Frau Wolfensohn-Kriss: Ueber den Blutdruck im Kindesalter. Arch. f. Kinderh., liii, Nos. 4-6.

130 mm. H. W. Cook[9] who investigated the value of the blood-pressure as a guide to stimulation in sick children, says that normal pressure in children varies rather widely because of many factors, including height, weight, and size of the arm, and although such a pressure may be called high for a child of a certain age, and another low, each reading must be judged by the circumstances of the case. Cook, however, did not attempt to find any relation between these factors. In fact, no one did until Frau Wolfensohn[8] in 1910 studied the relation between height and weight and blood-pressure. She draws the following conclusions from the study of 350 children:

1. Blood-pressure increases with age.
2. Blood-pressure increases with height and weight.
3. Children of the same age but of different weights and heights have different blood-pressures.
4. Sex is of no importance. Boys and girls show the same blood-pressure if their heights and weights are the same.

In the following study I have taken not only the weight and height into account, but also the circumference of the arm and have, according to Sallom's[10] method, in adults, estimated the pressure per square millimeter in the hope of obtaining a more accurate standard for normal children. I used Cook's modification of the Riva Rocca instrument with a cuff of 9 cm. width. I did not forget von Recklinghausen's[11] observation that errors are frequently due to a too narrow armlet, and that one narrower than 10 cm. should never be used. However, in the examination of a number of children it was found that the readings averaged only 5 mm. lower with the wider than with the narrower cuff, which is much more easily adjusted on their small arms. The children were seated at a low table, the cuff smoothly adjusted around the arm and connected with the mercurial manometer. Pressure was exerted until the pulse disappeared, then greater pressure was exerted until the mercury was far above the point of disappearance of the pulse. It was then allowed to drop until the pulse was again palpable. The point of disappearance and reappearance usually corresponded, and registered the systolic pressure.

In all, 128 normal children were examined, some several times to gauge the accuracy of results. The readings were taken as nearly as possible at the same time of day and under the same conditions, and the height, weight, and arm circumference measured. First, as to weight and height, just as in Frau Wolfensohn's experience, it can be seen from

9. Cook, H. W.: Clinical Value of Blood-Pressure Determinations as a Guide to Stimulation in Sick Children, Am. Jour. Med. Sc., 1903, p. 483.

10. Sallom, A. K.: Standardization of Blood-Pressure. New York Med. Jour., Sept. 24, 1910.

11. Von Recklinghausen: Arch. f. Exper. Path u. Pharm., 1902, xlvi, 78.

the following tables that there was apparently an increase in pressure with the increase in height and weight.

TABLE 1.—COMPARISON OF HEIGHT AND SYSTOLIC BLOOD-PRESSURE

Height.	Systolic Blood-Pressure. Mm.
3 ft. 6 in.	99
4 ft. to 4 ft. 3 in.	109
4 ft. 3 in. to 4 ft. 6 in	112
4 ft. 6 in. to 4 ft. 9 in	118
4 ft. 9 in. to 5 ft.	120
5 ft.	125

TABLE 2.—COMPARISON OF WEIGHT AND BLOOD-PRESSURE

Weight, Pounds.	Blood-Pressure, Mm.
30 to 40	95
40 to 50	100
50 to 60	107
60 to 70	112
70 to 80	116
80 to 90	122
90 to 100	126

I say apparently, for, when the circumference of the arm is measured and the blood-pressure per square millimeter is estimated, according to Sallom's[10] method, it is seen that the actual blood-pressure is practically the same for a 5-year-old child of 3 ft. 6 in., weighing 40 pounds, and a 15-year-old child of 4 ft. 8 in. weighing 90 pounds.

In a recent article on blood-pressure in adults A. K. Sallom[10] says that the area on which the pressure is exerted must be considered in estimating blood-pressure, for it is a law of physics that pressure exerted by any fluid depends on the height and width of the base. The actual blood-pressure then must equal the height of the mercurial column, divided by the width of the cuff, multiplied by the circumference of the arm. For example, A. K., blood-pressure 120 mm.; arm circumference 183 mm. × 90 mm., the width of the cuff equals 16,470 square mm.; then if 16,470 square mm. will sustain 120 mm. of mercury, 1 square mm. will sustain $120 \div 16{,}470 = .0072$ mm., which represents the actual blood-pressure.

In the 128 children examined this formula did not vary more than .0014 mm. Ten showed a blood-pressure per square mm. of .0070 mm. of mercury; ten of .0071 mm.; ten of .0072; eight of .0073; twelve of .0074; fourteen of .0075; twenty of .0076; twelve of .0077; fifteen of .0078; eleven of .0079 and six of .0080 to .0084 mm. The procedure is not so complicated as appears at first glance. Of course, one must always use a cuff of the same width in order to obtain uniform results, and must know what the normal for this width is. Then with a little experience the examiner knows as soon as the arm measurement and height of the

column of mercury are taken, whether the blood-pressure is high or low; or if he is not quite sure, it takes only a minute to make the calculation. He soon learns, also, to know about how many millimeters too high the mercurial column is to give the normal quotient when divided by the circumference of the arm times the width of the cuff; so that he can say such a child has a blood-pressure of 20, 30 or 40 mm. (as the case may be) above or below normal.

Thus we have a standard by which blood-pressure can be expressed, and the measurement of blood-pressure will serve not only as a guide for stimulation, as suggested by Cook and Howland,[12] and for prognosis in the acute infectious diseases, as suggested by Weigert,[13] but it will also give valuable physical information as to the circulation in all abnormal conditions.

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12. Howland, J.: Circulatory Failure in the Acute Infections of Children, Arch. f. Pediat., May, 1910.

13. Weigert, K.: Ueber das Verhalten des arteriellen Blutdrucks bei den infectiöse Krankheiten, Samml. Klin. Vortr., 1903, p. 80.

SPONTANEOUS HEMORRHAGE IN THE NEW-BORN*

WITH THE REPORT OF NINE CASES

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I. INTRODUCTION

There are few diseases or conditions in infancy which have attracted more attention than the hemorrhages which occur during the first two weeks of life. The enormous literature devoted to this subject consists in part of case reports and collected statistics bearing on the frequency, the etiology, and the treatment, and in part, of investigations concerning the exact causation of the bleeding.

The anatomic lesions disclosed by post-mortem examination have been inconstant, and divergent views have been held by different observers concerning the causation of the hemorrhage. The so-called hemorrhagic disease of the new-born has been attributed to general diseases, inherited or acquired; to birth injuries; to mechanical causes; and to primary defects or alterations of the blood or vessels.

Within the last few years there have been a number of important investigations on the physiology of the blood, and on the etiology and treatment of various hemorrhagic conditions. It seems that a revision of our ideas concerning the whole group of hemorrhagic diseases is at hand.

A review of the literature, and a study of nine cases of spontaneous hemorrhage in new-born infants, serve as the basis of this communication.

II. CLASSIFICATION

The hemorrhages which occur during the first few days of life may be traumatic, accidental, or spontaneous. The traumatic hemorrhages are usually due to injuries received during labor or consequent on some operative procedure.

The term accidental may be applied to two varieties of hemorrhage: first, the hemorrhage which may be due to inadequate ligation of the umbilical cord; and second, the slight vaginal bleeding which gives rise to no apparent symptoms and is unaccompanied by bleeding from other sources.[1] The latter is termed physiologic by Lequeux.[2]

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1. According to Eröss (Casuistischer Beitrag zur Pathologie der genitalen Blutungen neugeborenen Mädchen, Arch. f. Kinderh., 1891, xiii, 172), vaginal bleeding in the new-born may occur in association with multiple hemorrhages due to lues, sepsis, etc., but in most instances the vaginal hemorrhage is of no patho-

Judging from published reports, spontaneous hemorrhage may arise from almost any organ or tissue and may be associated with different pathologic conditions. In general, two different classifications have been followed. In some instances the classification is based on the apparent origin of the hemorrhage; in others, an etiologic classification has been attempted.

The whole group of hemorrhages has been included under the *hemorrhagic diathesis* or *disease of the new-born,* or *hemophilia neonatorum.*

According to the origin of the hemorrhage, cases are described as melena, purpura,[3] cerebral, umbilical, hepatic or adrenal hemorrhage. In many cases the greater part of the external hemorrhage is from the umbilical cord or from the gastro-enteric tract and the terms melena and omphalorrhagia have been used in a generic sense.

The cases of melena are subdivided into: melena symptomatica, when the hemorrhage is the symptom of some obvious disease; melena spuria, when the blood vomited or in the stools is from sources other than the gastro-enteric tract; and melena vera or idiopathica, when there is no apparent cause for the hemorrhage.

Similarly, the term omphalorrhagia idiopathica has been used for umbilical hemorrhage of obscure causation. Runge[4] divides the umbilical hemorrhages into two groups. In the first group the hemorrhage is from the lumen of the vessels and may occur (a) before, or (b) after, the separation of the cord. The hemorrhage in the second group is parenchymatous and takes place by oozing as though the blood were "squeezed from a sponge."

The terms melena and omphalorrhagia thus applied do not refer merely to the origin of the hemorrhage, but are descriptive of clinical groups of cases. Although in many instances the external hemorrhage is from a single source, post-mortem examination often shows that the hemorrhage was of multiple origin. Moreover, the clinical picture as evi-

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logic significance. Jardine (Vaginal Hemorrhage in the New-born, Brit. Med. Jour., 1897, ii, 652), and many others have reported cases which show the benign nature of vaginal bleeding in the new-born. This variety of vaginal hemorrhage occurred in thirty-five of 10,000 female infants observed by Shukowsky (Metrorrhagia Neonatorum, Jahrb. f. Kinderh., 1903, lviii, 105). Ribemont (Des hémorrhagies chez le nouveau-né, Paris, 1880), collected nineteen cases of benign vaginal bleeding in the new-born in which the patients were observed from three months to twelve years. In seven instances the hemorrhage recurred at more or less regular intervals; in three cases the hemorrhage reappeared one or more times, but at irregular periods, while in nine cases there was no recurrence of the bleeding.

2. Lequeux: Etiologie et pathogénie des hémorrhagies graves du nouveau-né. Paris Thesis, 1906.

3. Allan: Two Cases of Purpura Hemorrhagica Neonatorum, Glasgow Med. Jour., 1907, lxviii, 155.

4. Runge: Die Krankheiten der Ersten Lebenstage, Stuttgart, 1885.

denced by the onset, the course, and the severity of the hemorrhage, is frequently the same, no matter whether the bleeding is external, from the umbilical cord, the mucous membranes, the skin, or from the internal organs.

Our present knowledge does not admit of an accurate etiologic classification, but from a purely clinical standpoint the spontaneous hemorrhages are separated into two groups. The first group comprises the cases in which the hemorrhage appears as an incident during the course of some definite disease, the symptoms of which are apparently dependent on a general pathologic process. In a second group of cases the hemorrhage dominates the entire clinical picture; the symptoms, and the fatal outcome, when such occurs, are directly referable to the loss of blood. It is with the latter group of cases that this paper is particularly concerned.

III. SYMPTOMATOLOGY

The hemorrhage usually occurs before the tenth day of life and most commonly on the second or third day. The time of onset depends somewhat on the source of bleeding and also on the associated pathologic condition—when such exists.

Premonitory symptoms are often present. The infant cries more than usual, is restless, and refuses to nurse. In many cases of melena there is evidence of abdominal pain. Fever is often present and vomiting or diarrhea may occur. The temperature is influenced to a considerable degree by the type and severity of the hemorrhage. Although the temperature is often elevated at the onset, it usually falls with the occurrence of severe hemorrhage and becomes subnormal when much blood has been lost. The symptoms may be present from one to twenty-four hours before the appearance of the blood. In many cases, however, premonitory symptoms are absent, or the symptoms are so slight that they do not attract attention at the time.

The course and extent of the bleeding are also variable. The hemorrhage may be slight and continuous, or it may be intermittent. In many cases the external hemorrhage is of multiple origin and is very often associated with internal hemorrhage of varying severity. As shown by Lequeux[2] and others, there may be extensive internal hemorrhage while the external hemorrhage is slight or even absent (Cases 8 and 9, Young and Richards[5]). In some cases the hemorrhage is of sudden onset and causes almost immediate death. This type is most common in the massive hemorrhages into the liver, the lungs, or the adrenal glands.

There is no definite clinical type to which the cases conform. When general symptoms or signs are present they are usually due to some gen-

5. Young and Richards: Hemorrhagic Disease of the New-born, Boston Med. and Surg. Jour., 1910, clxii, 47.

eral disease, of which the hemorrhage is one of the manifestations. The only feature common to all cases is the loss of blood and the resulting anemia.

IV. FREQUENCY

The frequency with which spontaneous hemorrhage occurs in the newborn, varies in the experience of different observers. According to Silvermann[6] there were thirty-seven cases of gastro-enteric hemorrhage in a total of 29,333 births, and according to Kling[8] seventeen cases occurred in between 12,000 and 13,000 births. Herrgott[7] observed two cases in 3,000 births, Holtzschmidt[9] had fourteen cases from 14,203 births and Shukowsky[10] observed twenty-nine cases in 30,000 births.

According to Winkel,[11] Gerhardt[12] and Ribemont,[13] umbilical hemorrhage occurs once for each 5,000 births. Nohl[14] cites a ratio of one case to 1,816 births and Orlowsky[15] one case to 116 births.

V. ETIOLOGY

During the earlier periods of investigation the so-called hemorrhagic disease was ascribed to widely varying causes. Among these are asphyxia from prolonged labor, general plethora, congestion of the mesenteric arteries, respiratory embarrassment, vascular thrombosis, rupture of blood-vessels, irritation due to swallowed amniotic fluid, and too early ligation of the umbilical cord. Later, the occurrence of melena was explained by some observers on the basis of inflammation of the gastro-enteric tract; by others, the bleeding was thought to originate from ulcers or erosions of the mucous membrane.

In 1871, Grandidier[16] considered that a persistence of the ductus arteriosus and the foramen ovale were factors in the occurrence of umbilical hemorrhage.

Hemophilia. By many of the earlier writers hemophilia was considered an important cause of severe spontaneous hemorrhage in the newborn. *Hemophilia neonatorum* is often used as a generic term for the

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6. Silvermann: Quoted by Shukowsky (see Note 10).
7. Herrgott: Quoted by Shukowsky (see note 10).
8. Kling, Lorenz: Ueber Melaena neonatorum; Inaug. Dissert., München, 1875.
9. Holtzschmidt: Melena Neonatorum, München. med. Wchnschr., 1902, xlix, 13.
10. Shukowsky: Melena neonatorum; Magendarmblutungen bei Neugeborenen, Arch. f. Kinderh., 1907, xlv, 321.
11. Winkel: Quoted by Lequeux (see note 2) and by Nohl (see note 14).
12. Gerhardt: Quoted by Lequeux (see note 2) and by Shukowsky (see note 10).
13. Ribemont: Quoted by Lequeux (see note 2) and by Shukowsky (see note 10).
14. Nohl: Gelatinbehandlung der Melaena neonatorum vera und der Omphalorrhagia idiopathica: Inaugural Dissertation, Berlin, 1910.
15. Orlowsky: Quoted by Lequeux (see note 2) and by Shukowsky (see note 10).
16. Grandidier: Die Freiwilligen Nabelblutung in der Neugeborenen, Cassel, 1871.

whole group of spontaneous hemorrhages. As a generic term it is inaccurate and adds confusion, for the greater number of these hemorrhages have no relation to true hemophilia. In most instances hemophilia is not manifested in the new-born. A few cases have been reported, however, which indicate that true hemophilia is sometimes the cause of severe hemorrhage during the first two weeks of life.

There was a family history of hemophilia in fourteen (6 per cent.) of the cases of spontaneous hemorrhage collected by Grandidier in 1871. Wittner[17] observed severe hemorrhage after circumcision in an infant with a definite family history of bleeding. Two brothers and eight uncles had died from hemorrhage following the same operation. Larrabee[18] has collected thirty-seven cases in which hemophilia was the apparent cause of hemorrhage in the new-born. Cases were accepted as hemophilia "(a) if there was a distinct history of this disease in the family, or (b) if the baby recovered from the first hemorrhage, but in after life remained a bleeder." The term hemophilia neonatorum should be restricted to this small group of cases.[19]

Bacterial Infection. It has long been recognized that many infectious diseases may present hemorrhagic types and there is considerable evidence to show that bacterial infection may be responsible for hemorrhage in the new-born. This evidence is of both clinical and bacteriologic nature. It was observed by Scanzoni[20] and others that hemorrhage was more common in infants during the prevalence of puerperal infection. According to Nicholson,[21] out of 1,500 births at Sloan Maternity Hospital during a period free from puerperal infection, there were no cases of hemorrhage, but in a subsequent 225 deliveries during the prevalence of puerperal

17. Wittner: Ein Fall von Hämophilie bei einem Neugeborenen, Abstr. Jahrb. f. Kinderh., 1899, i, 178.

18. Larrabee: Hemophilia in the Newly-Born with Report of a Case, Am. Jour. Med. Sc., 1906, cxxxi, 497.

19. There is a variety of severe hemorrhage in the new-born which is perhaps closely related to hemophilia. In the reported cases there was no family history of bleeding, but uncontrollable hemorrhage followed slight surgical operations, such as retraction of the prepuce, circumcision, and cutting the frenum linguæ. Cases of this sort have been observed by Ziegel (A Case of Hemophilia Neonatorum, Arch. Pediat., 1908, xxv, 120), Brittin (A Case of Hemophilia Neonatorum, Lancet, London, 1908, ii, 158), and others. Ribemont (See note 1) cites a number of cases in which severe hemorrhage followed slight surgical operations. The possibility of an acquired tendency to bleeding which persists, and is therefore closely related to true hemophilia, cannot be denied, for such cases have been observed by Horder, White (Cases of Acquired Hemophilia, Lancet, London, 1909, ii, 1611), and others.

20. Scanzoni: Quoted by Lequeux (see note 2).

21. Nicholson: Report of a Case of Melena Neonatorum Due Apparently to an Infection by the Bacillus pyocyaneus, Am. Jour. Med. Sc., 1900, cxx, 417.

infection, there were eight cases of hemorrhage. Townsend[22] and Ritter[23] observed that hemorrhage occurs with much greater frequency in infants born in maternity hospitals than in private practice. Townsend's statistics show that hemorrhage occurred in 0.67 per cent. of the infants delivered in hospital, while in the out-patient department the incidence of hemorrhage was only 0.1 per cent.

There have been a number of epidemics among the infants in maternity hospitals during which hemorrhage was a frequent symptom. Lequeux[2] describes an epidemic of streptococcic septicemia during which fourteen infants died within a period of twenty-four days. In six of the cases there were definite hemorrhages.

In the epidemic observed by Kilham and Mercealis[24] at the New York Infirmary for Women and Children in 1897, hemorrhage occurred in 18 per cent. of the infants born from February 19 to May 1. At the time there were no cases of puerperal infection in the ward; the cases of hemorrhage occurred in rapid succession, and ceased after the enforcement of proper isolation.

Klebs,[25] Ritter,[23] and Ebstein[26] observed cases of multiple hemorrhage in the new-born which followed suppuration of the umbilical cord. There was evidence of septicemia in twenty-one of the fifty-one cases of hemorrhage in the new-born observed by Ebstein.

In 1875 Klebs[25] described an organism, called by him the *Monas hemorrhagicum,* which he found in the tissues of an infant who had hemorrhage during life. A little later, Eppinger[27] discovered what was apparently the same organism in the viscera of an infant who had multiple hemorrhages. Weigert,[28] in a case of umbilical infection, found micrococci in hemorrhagic areas in the lungs and kidneys. Rehn,[29] in 1878, found micro-organisms in hemorrhagic ulcers of the stomach in a new-born infant. In 1889, Baginski[30] isolated *Streptococcus pyogenes* from a case of pyemia with hemorrhagic manifestations.

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22. Townsend: The Hemorrhagic Disease of the New-Born, Arch. Pediat., 1894, xi, 559.

23. Ritter: Blutungen im frühesten Kindesalter, Oest. Jahrb. f. Pädiat., 1871, ii, 127; Das Verhältniss der Temporären Hämophilie der Neugeborenen zu Blutungen im Späteren Alter und zu der Blutkrankheit, Prag. med. Wchnschr., 1877, ii, 425 and 445.

24. Kilham and Mercealis: Hemorrhagic Disease of the New-Born, A Report of Ten Cases, Arch. Pediat., 1899, xvi, 161.

25. Klebs: Kenntniss der pathogene Schistomyceten, Arch. f. exper. Path. u. Pharmakol., 1875, iv, 409.

26. Ebstein: Quoted by Runge (see note 4).

27. Eppinger: Beitrag zu den mycotischen Erkrankungen. 1. Hämophilia Neonatorum. Prag. med. Wchnschr., 1877, ii, 794, 814 and 841.

28. Weigert: Quoted by v. Dungern (note 33) and by Finkelstein (note 31).

29. Rehn: Quoted by v. Dungern and by Finkelstein.

30. Baginski: Quoted by v. Dungern (note 33).

Following these observations a number of organisms were isolated in rapid succession from the blood and organs of infants who had hemorrhage during life. The hemorrhages of infectious origin are divided by Finkelstein[31] into two groups. In the first group are the cases in which the hemorrhage has been ascribed to pyogenic organisms. In some cases there has been definite evidence of pus formation, either in connection with localized suppuration, or as a part of general pyemia. In other cases the pus cocci either alone, or in connection with saprophytic organisms such as the *Bacillus pyocyaneus* or some member of the proteus group, have been held responsible for hemorrhagic forms of septicemia.

In the second group of cases, specific hemorrhage-producing organisms are described as the causative agent. Babes[32] described such an organism in 1891 and v. Dungern,[33] Gärtner,[34] Lubarsch,[35] Babes[32] and Finkelstein,[31] Kilham and Mercealis,[24] Mapes,[36] and Nicholson,[21, 37] have isolated organisms of this sort from cases of the so-called hemorrhagic disease. In most instances these organisms produced hemorrhagic inflammation, or hemorrhagic forms of septicemia when injected into rabbits or guinea-pigs.

The results of the bacteriologic studies have been very inconstant; the pus cocci, the colon bacillus, the typhoid bacillus, *Bacillus enteritidis, Bacillus lactis aerogenes,* the diphtheria bacillus, the *Bacillus hemorrhagica* of Kolb, the pneumococcus, the pneumobacillus of Friedlander, and several unclassified organisms, have been recovered, either singly or in combination, from the bodies of infants who had hemorrhage during life. It is thus seen that no specific bacterial cause has been discovered. The multiplicity of organisms, and the comparative infrequency with which different observers have isolated the same organism—excepting perhaps the pus cocci—merely indicate that hemorrhage in the new-born may occur during the course of bacterial infection.

There is, in addition, a serious objection to many of the bacteriologic examinations. The evidence in most cases rests on post-mortem examination, which was often made from twelve to twenty-four hours after death. The presence of bacteria in some of these cases may have been due to post-mortem invasion.

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31. Finkelstein: Lehrbuch der Säuglingskrankheiten, 1905, first half, 98.
32. Babes: Ueber Bacillen der hämorrhagischen Infektion des Menschen. Centralbl. f. Bakt. u. Parasitenk., 1891, ix, 719.
33. Von Dungern: Ein Fall von hämorrhagische Sepsis beim Neugeborenen, Centralbl. f. Bakt. u. Parasitenk., 1893, xiv, 541.
34. Gärtner: Identischer Bakterienbefund bei zwei Melaenafallen Neugeborener, Arch. f. Gynäk., 1894, xlv, 272.
35. Lubarsch: Quoted by Finkelstein (see note 31).
36. Mapes: Quoted by Holt, The Diseases of Infancy and Childhood, 1903, page 100.
37. Hamill and Nicholson: Infections of the Newborn, Arch. Pediat., 1903, xx, 641.

From a clinical standpoint, most of the cases for which the bacteriologic evidence is strongest belong to the group in which hemorrhage is one of the manifestations of a recognized type of bacterial infection. The presence of some general pathologic process is often shown by fever, of a remittent or intermittent type, jaundice, general symptoms, toxemia and, in some cases, evidence of pus formation. Of the same significance is the post-mortem evidence of bronchopneumonia or general pyemia. The bacteriolytic examination has been positive in comparatively few of the cases in which in the absence of general symptoms, the hemorrhage was of sudden onset during the first three days, and the only important objective sign was the loss of blood and the resulting anemia.

Syphilis. Perhaps of next importance to bacterial infection as a cause of hemorrhage in the new-born, is congenital syphilis. In 1876, Epstein[38] referred to congenital lues as a cause of hemorrhage in the new-born, probably induced by changes in the capillary walls. Behrend[39] came to the same conclusion and used the term "syphilis hemorrhagica neonatorum" to describe a group of cases in which hemorrhage occurred in connection with well-defined luetic lesions. Shutz[40] and Esser[41] also considered that the lesions of congenital syphilis were a frequent cause of hemorrhage in the new-born.

The presence of vascular changes was denied by Fischl[42] who doubted the importance of syphilis as a direct cause of hemorrhage. The views of subsequent writers show considerable divergence, and it is perhaps best to cite some of the evidence on which these views were based. Kassowitz and Hochsinger[43] in 1886 found micrococci in the organs of infants with congenital syphilis. Kolisko,[44] in the same year, and Chotzen[45] in 1887 confirmed these observations and concluded that the feeble resisting power of the infants constituted a predisposition to bacterial infection. Later, Neumann,[46] Peterson,[47] Finkelstein,[31, 48] and others, recovered

38. Epstein: Quoted by Runge (see note 4).

39. Behrend: Quoted by Finkelstein (note 31) and by Mracek (see note 54).

40. Shutz: Quoted by Finkelstein (note 31) and by Mracek (see note 54).

41. Esser: Enteritis Syphilitica unter dem Bilde der Melaena Neonatorum, Arch. f. Kinderh., 1901, xxxii, 177.

42. Fischl: Zur Kenntniss d. hämorrhagische Diathese hereditär-syphilit. Kinder, Arch. f. Kinderh., 1887, viii, 10.

43. Kassowitz and Hochsinger: Ueber einen Mikroorganismus in den Geweben hereditär-syphilit. Kinder, Wein. med. Blatt., 1886, ix, 1, 34, and 70.

44. Kolisko: Ueber den Kassowitz-Hochsinger'schen Micrococcenbefund bei Lues congenita, Wien. med. Blatt, 1886, ix, 97 and 133.

45. Chotzen: Ueber Streptococcen bei hereditär-syphilit. Vierteljahressch. f. Dermat. u. Syph., 1887, xiv, 109.

46. Neumann: Fall von Melaena Neonatorum mit Beimerkungen über die hämorrhagische Diathese Neugeborener, Arch. f. Kinderh., 1891, xii, 54; 1891, xiii, 211.

47. Peterson: Quoted by Finkelstein (note 33) and by Mraček (see note 54).

48. Finkelstein: Ein Fall von hämorrhagische Diathese, Berl. klin. Wchnschr., 1895, xxxii, 497.

bacteria from the blood and organs of congenital syphilitic infants who had hemorrhage during life. They concluded that hemorrhage due to congenital syphilis alone does not occur. Simon,[49] Henoch,[50] Hamill and Nicholson,[37] and others held the same view and considered that congenital syphilis was merely a predisposing factor to bacterial infection — the direct cause of the hemorrhage.

On the other hand, Wilson[51] believes that congenital syphilis is an important cause of the so-called hemorrhagic disease. There was a definite history of syphilis in one of the parents, or evidence of the disease in the infant, in ten out of forty-five cases of hemorrhage cited by Wilson. Hess[52] and Escalon[53] also believe that in some cases congenital syphilis may be the sole cause of hemorrhage.

The main objections which have been raised to congenital syphilis as the direct cause of hemorrhage in the new-born are as follows: (1) that some observers were unable to demonstrate vascular changes in syphilitic infants; (2) that congenital syphilitic infants are predisposed to bacterial infection; (3) that bacteria have been found in some cases of hemorrhage in infants suffering from congenital syphilis.

There are, however, a number of observations which indicate that these objections are not applicable to all cases. In 132 autopsies on congenital syphilitic infants studied by Mracêk,[54] hemorrhage of some grade was found in forty-four, or one-third of the cases. The cases were divided into two groups. In one group there were twenty-three cases in which the hemorrhage was confined to a small part of the body or to a single organ. This group was termed "hemorrhage in syphilitic infants." The second group comprised nineteen cases of multiple hemorrhage to which the term "syphilis hemorrhagica neonatorum" was applied. In these nineteen cases, ten of the mothers had well-defined secondary lesions at the time of confinement. The remaining nine had syphilis shortly before confinement and showed residua in the form of scars, pigmentation, and glandular enlargement. To none of the mothers had thorough treatment been given. The liver, lungs and epiphyses of the infants showed the characteristic syphilitic lesions. Mracêk was able to demonstrate changes in the smaller veins and capillaries and the bacteriologic examination made in four cases by Paltauf and Kolisko was negative.

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49. Simon: Quoted by Finkelstein (see note 33).
50. Henoch: Vorlesungen über Kinderkrankheiten, Berlin, 1893.
51. Wilson; Hemorrhage of Syphilitic Origin in the New-born, Arch. Pediat., 1905, xxii, 43.
52. Hess: Syphilis Hemorrhagica Neonatorum, Arch. Pediat., 1904, xxi, 598.
53. Escalon: Des Hémorrhagies gastrointestinales des noveau-nés. Abstr. Centralbl. f. Gynäk., 1908, xxxii, 1679.
54. Mracêk: Syphilis Hämorrhagica Neonatorum, Vierteljahressch. f. Dermat. u. Syph., 1887, xiv, 117.

Cases have been collected by Lequeux[2] and others in which hemorrhage occurred in luetic infants in the presence of a negative bacteriologic examination. Swartz and Ottenberg[55] have recently reported a case of multiple hemorrhage in a luetic infant in which an *intra vitam* blood-culture was negative. The liver and spleen were enlarged, spirochetes were demonstrated in the former, and a positive Wassermann reaction was obtained in the cerebrospinal fluid.

In most of the reported cases the diagnosis of syphilis was based on the family history, or on the anatomic evidence of the disease. We have observed two cases of hemorrhage in the new-born in which a positive Wassermann reaction suggested syphilis as an etiologic factor. Both cases terminated in recovery and neither showed any clinical sign of the disease. In one case (Case 3) the syphilitic origin of the hemorrhage is supported by the apparent influence of mercurial therapy; in the other (Case 1) by a negative blood-culture.

Judging from the evidence which has been quoted, it seems that most writers agree that congenital syphilis is a predisposing cause of hemorrhage. Whether the lesions of syphilis may be the sole cause, is a disputed question, but the available evidence indicates that in some cases, at least, congenital syphilis is the only determinable factor.

Cerebral Injury. The view that cerebral injury is an important cause of melena in the new-born is advocated by Pomorski[56] and v. Preuschen.[57] Pomorski extended the observations of Brown-Séquard, Schiff, Ebstein and Klosterhalfen and found that various brain injuries in dogs gave rise to hyperemia and hemorrhage in the lungs and to hyperemia, hemorrhage and ulceration in the stomach. Von Preuschen found cerebral hemorrhage in two cases of melena and in collected statistics he noted that of forty-six cases of melena the labor had been difficult or prolonged in thirty-two. He also found that cerebral hemorrhage was present in three of the five cases in which the brain had been examined.

It is difficult to judge the value of this hypothesis. A number of cases have been reported in which hemorrhage was found in various parts of the brain, and in which there was no evidence of gastro-enteric hemorrhage (Couvelaire[58]). Cases of melena have also been observed in which there was no evidence of brain injury. It therefore seems improbable that cerebral injury is a constant, or even frequent, cause of gastro-

55. Schwarz and Ottenberg: The Hemorrhagic Disease of the New-Born, with Special Reference to Blood Coagulation and Serum Treatment, Am. Jour. Med. Sc., 1910, cxl, 17.

56. Pomorski: Experimentelles zur Aetiologie der Melaena neonatorum, Arch. f. Kinderh., 1892, xiv, 165.

57. von Preuschen: Melaena neonatorum. Centralbl. f. Gynäk., 1894, xviii, 201.

58. Couvelaire: Hémorrhagies du système nerveaux cérébral des nouveau-nés, Ann. de gynec. et d'obst., 1903, lix, 253.

enteric hemorrhage in the new-born, but it is possible that some cases are of such origin.

Local Causes. In addition to the general causes which have been considered, there are certain local causes which have been considered responsible for hemorrhage during the first week of life. The most common is ulceration in some part of the gastro-enteric tract. Billard[59] in 1828 referred to cases in which ulceration of the stomach or duodenum was found on post-mortem examination, and similar cases have been cited by Landau,[60] Dusser,[61] Bauer,[62] Goodheart,[63] Grainger-Bisset,[64] Chrzanowski,[65] Silbermann,[66] Spiegelberg,[67] Rheiner,[68] Hecker[69] and many others. The ulcers are most common in the stomach or duodenum, but sometimes occur in the lower part of the esophagus. In some instances the ulcers are of considerable size and present the same general appearance as those found in adults. Fenwick[70] in 1900 was able to collect reports of eighteen cases of definite gastric ulcer in infants and young children. Bauer described a case of gastro-enteric hemorrhage in a new-born infant apparently due to a punched out gastric ulcer 4 by 3.4 mm. in diameter. Goodheart described a somewhat similar case in which the eroded vessel could be seen in the base of the ulcer. Landau cites a case of duodenal ulcer with fatal hemorrhage due to erosion of a branch of the gastroduodenal artery. The ulcer measured 8 by 6 mm. In Hecker's case two ulcers were found, one of which had a diameter of 1.5 cm. In many of the reported cases the ulcers were very small and in some instances were only of microscopic size. In other cases hemorrhagic erosions were present.

In cases of melena the gastro-intestinal mucous membrane may be intensely congested, and Shukowsky[10] believes that gastro-enteric hemorrhage is often due to hemorrhagic gastro-enteritis or ileocolitis.

Blood or Vascular Changes or Defects. In addition to the etiologic factors which have been considered, the ultimate cause of the uncontrol-

59. Billard: Traité des maladies des enfants nouveau-nés, etc., Paris, 1828.
60. Landau: Ueber Melaena des Neugeborenen, etc., Breslau, 1874.
61. Dusser: Quoted by Pomorski (note 56) and by Finkelstein (see note 33).
62. Bauer: Zur Aetiologie der Melaena neonatorum, Centralbl. f. Gynäk., 1905, xxix, 1169; Münch. med. Wchnschr., 1904, li, 1207.
63. Goodheart: Tr. Lond. Path. Soc., 1881, xxxii, 86.
64. Grainger-Bisset: A Case of Perforated Gastric Ulcer with Fatal Hemorrhage from the Bowel in an Infant Forty-five Hours Old, Lancet, London, 1905, ii, 78.
65. Chrzanowski: Zwei Fälle von Malaena neonatorum, Abs. Jahrb. f. Kinderh., 1899, l, 176.
66. Silbermann: Ueber Melaena vera neonatorum, Jahrb. f. Kinderh., 1877, xi, 378.
67. Spiegelberg: Ein Fall von Melaena neonatorum, etc., Abs. Jahrb. f. Kinderh., 1899, l, 176.
68. Rheiner: Ueber Melaena neonatorum, Abs. Jahrb. f. Kinderh., 1899, l, 176.
69. Hecker: Quoted by Ribemont (see note 1).
70. Fenwick: Ulcer of Stomach and Duodenum and its Consequences, London, 1900.

lable hemorrhage is to be sought in some abnormal condition of the blood. It is a common observation in cases of hemorrhage in the new-born, that the blood may remain fluid many hours after death. In 1850, Bowditch[71] noted the lack of blood coagulation in a fatal case of umbilical hemorrhage. Weber,[72] in 1851, referred to the futility of local measures to control the hemorrhage and noted that there was a great delay, if not an entire absence, of coagulation in the flowing blood. In 1852, Minot[73] in describing the hemorrhagic diathesis of the new-born referred to "the thin watery condition of the blood, and its great deficiency in fibrin, whereby mechanical means become almost wholly inefficacious to arrest its flow." Wilson, Lucas,[74] and many other writers, have suggested that the continued hemorrhage was dependent on delayed or incomplete coagulation of the blood.

TABLE SHOWING TIME OF COAGULATION OF BLOOD DURING HEMORRHAGE AND AFTER RECOVERY IN SEVEN CASES

Case	Coagulation Time During Hemorrhage, Minutes	Coagulation Time After Recovery, Minutes
1.	No trace of coagulation at the end of 1½ hours.	4*
2.	Few fibrin flocculi at the end of ½ hour. No definite clot...	3 to 4*
3.	9†	8½†
4.	5¾†	7†
5.	9†	3¾†
6.	3½†	....
7.	6†	1½†

* Determined by Hinman and Sladen's modification of the method of Milian. In six normal new-born infants, the coagulation time with this method varied from four to five minutes (room temperature).

† By a slight modification of the method of Vierordt. Dr. H. Lett has found that with this method the normal coagulation time in the new-born is 2.3 to 3 minutes at a temperature of 35 to 40 C. (Personal communication.)

In one case observed by Finkelstein,[31] only slight signs of coagulation were noted after twelve hours; in a second case there was no trace of coagulation at the end of forty-eight hours. According to Finkelstein the main characteristics of the hemorrhagic diathesis of the new-born are the uncontrollable nature of the hemorrhage, and a loss or delay of blood coagulation. Luqueux[2] states that in these cases the clotting of the blood

71. Bowditch: On Hemorrhage from the Umbilicus in New-Born Children; with Cases. Am. Jour. Med. Sc., 1850, xix, 63.

72. Weber: Beiträge zur pathologischen Anatomie der Neugeborenen, Kiel, 1851.

73. Minot: On Hemorrhage from the Umbilicus in New-Born Infants; with an Analysis of Forty-Six Cases, Am. Jour. Med. Sc., 1852, xxiv, 310.

74. Lucas: Recent Experimental Work on Hemorrhagic Conditions, Boston Med. and Surg. Jour., 1909, clxi, 731.

is retarded, and the retraction of the clot, though not absent, is slow and often incomplete.

Schwarz and Ottenberg[55] have recently called attention to impaired blood coagulation as the immediate cause of uncontrollable hemorrhage in the new-born. From their experiments they considered that the impaired coagulability is probably due to a destruction of, or to interference with, the production of thrombokinase.

The coagulation time of the blood was determined in seven of our cases. The data are shown in the accompanying table.

The above results do not show a constant delay of blood coagulation. In cases 1 and 2, coagulation was greatly delayed if not entirely absent. In Cases 3 and 5 coagulation was slightly delayed; in Cases 4 and 7 the delay is questionable, while in Case 6 the coagulation time was normal.

This same variation is shown in the observations made after the cessation of the hemorrhage. After recovery, the coagulation time was normal in the two cases (1 and 2) in which it was previously greatly delayed or absent, and in one case (5) in which it had been slightly delayed. In one case (3), however, the coagulation time was practically the same during the bleeding and after its cessation, while in Case 4 the onset of coagulation was later, after the hemorrhage had ceased. In Case 7 the coagulation time was greatly decreased after recovery from the hemorrhage, though it was very slightly, if at all, delayed at the time of actual bleeding.

From these observations it seems that an absence, or a delayed onset of coagulation is not constant in the hemorrhagic conditions of the new-born. Lequeux observed a case of multiple hemorrhage in a new-born infant in which the blood coagulated completely in six minutes, the same time as a specimen of normal blood used as a control.

In our cases which showed a normal or only slightly delayed coagulation time, the readings were taken from the first appearance of clotting and no observations were made on the completeness of clot formation or on the clot retraction. It has been observed in other hemorrhagic conditions that the onset of coagulation may be within the normal time but that clot retraction is defective or absent. This condition has been attributed by Duke[75] and others to a lack of blood-platelets.

Whipple and Hurwitz[76] observed a marked tendency to continued bleeding in dogs suffering from necrosis of the liver due to chloroform poisoning. They found that there was a deficiency of fibrinogen, and though a loose-meshed clot was formed, it was unable to check even capil-

75. Duke: The Relation of Blood Platelets to Hemorrhagic Disease, Jour. Am. Med. Assn., 1910, lv, 1185.

76. Whipple and Hurwitz: Fibrinogen of the Blood as Influenced by the Liver Necrosis of Chloroform Poisoning, Jour. Exper. Med., 1911, xiii, 136.

lary hemorrhage. The hemorrhagic condition was therefore due to incomplete, rather than a lack of, blood-coagulation.

It is quite possible that incomplete, instead of delayed, coagulation is the underlying cause of the hemorrhage in some cases of continued bleeding in the new-born.

The delayed coagulation in Cases 1 and 2 was shown by the following experiments to be due to a deficiency or absence of thrombin:

Experiment 1.—Coagulation did not occur after the addition of calcium chlorid.

A deficiency of calcium was therefore not the cause of the delayed coagulation.

Experiment 2.—The addition of normal defibrinated human blood caused the infant's blood to coagulate completely in three to four minutes.

This experiment showed that there was no deficiency of fibrinogen, and also that an "antithrombin" was not the cause of the delayed blood coagulation. The defibrinated blood is supposed to contain thrombin and thrombokinase, either (or both) of which was responsible for the coagulation of the infant's blood.

Experiment 3.—Defibrinated human blood which had been heated to 60 to 63 C. for thirty-five minutes to destroy the preformed thrombin caused the infant's blood to clot in six to seven minutes. Coagulation, however, was incomplete and the resulting clot soft and gelatinous.

These results suggest a blood state similar to that found by Sahli[77] in hemophilia, which results were interpreted to indicate a deficiency of thrombokinase.[78] The evidence for this view is not conclusive, however, for Howell[79] has recently obtained a pure thrombin which under certain conditions is not destroyed by heat even greater than that used in the third experiment. It is possible that the preformed thrombin is not destroyed by this amount of heat and that the activity of the defibrinated blood was still due to thrombin and not necessarily to thrombokinase.

In addition to a deficiency of thrombin or its precursors (prothrombin and thrombokinase), defective blood-coagulation may be due to inhibiting substances or "antithrombin," to a deficiency or inavailability of calcium salts, or to a lack of fibrinogen. Any of these factors may therefore be responsible for uncontrollable hemorrhage. The observations on the blood state in the hemorrhagic conditions of the new-born are too meager to show whether the hemorrhage is always dependent on a single factor,

77. Sahli: Ueber das Wesen der Hämophilie, Ztschr. f. klin. Med., 1905, lvi, 264; Weitere Beiträge zur Lehre von der Hämophilie, Deutsch. Arch. f. klin. Med., 1910, xcix, 518.

78. From the results of a different method of investigation, Addis (Hemophilia, Brit. Med. Jour., 1910, ii, 1422) believes that the blood defect in hemophilia lies in the activation of prothrombin rather than in a deficiency of thrombokinase.

79. Howell: The Preparation and Properties of Thrombin, Together with Observations on Antithrombin and Prothrombin. Am. Jour. Physiol., 1910, xxvi, 253.

or whether the blood defect varies in different cases. A consideration of the fact that the coagulation time is normal in some of the cases and greatly delayed in others, and that hemorrhage in the new-born is due apparently to different pathologic conditions, suggests that the cause of the persistent bleeding is not uniform.

It seems highly probable that vascular lesions play an important part in the production of hemorrhage. The exact pathology, however, is not well understood.

The coagulation of the blood is apparently the normal mechanism for the control of hemorrhage, a defect of which would give rise to persistent bleeding. But it is difficult to understand how a reduction of the blood coagulability can be sufficient in itself to inaugurate the bleeding. The immediate cause of the hemorrhage is probably dependent on some vascular lesion; the uncontrollable nature of the bleeding on defective blood-coagulation.

By some writers vascular lesions have been considered a cause of hemorrhage in congenital syphilis. In the presence of defective blood-coagulation, it is probable that uncontrollable hemorrhage may result from slight traumatic lesions which under other circumstances would be of no consequence. Injuries to the vessel wall may be due to infective emboli and to inflammation. It is also possible that toxic agents may produce vascular lesions sufficient to give rise to hemorrhage.*

It has been mentioned that severe spontaneous hemorrhage in the new-born has been attributed to bacterial infection, to inherited syphilis, to cerebral injury and to local causes such as ulceration and acute congestion. It seems that in the new-born infant there is a general predisposition to severe and uncontrollable hemorrhage for which different agencies may serve as the exciting cause.

There is a type, however, of severe spontaneous hemorrhage, of sudden onset, of short clinical course, without signs other than those dependent on the hemorrhage, for which no definite cause has been demonstrated. The question naturally arises whether these cases might not depend entirely on some primary deficiency of the blood or vessels.

In consideration of the immediate curative effect of blood transfusion, Lambert[80] and Murphy[81] believe that in melena neonatorum there is a

* It has been shown that when the vessel wall is injured, a substance arises which has at least an accelerating action on blood coagulation (the zymoplastic substance or thrombokinase). (Bernheim: The Relation of the Vessel Wall to Coagulation of the Blood, Jour. A. M. A., 1910, lv, 283.) It is possible that this substance is of importance in causing thrombosis of the bleeding vessel and that a deficiency, or interference with the action of this substance may be a factor in the causation of persistent hemorrhage.

80. Lambert: Melena Neonatorum, With Report of a Case Cured by Transfusion, Med. Rec., 1908, lxxiii, 885.

81. Swain, Murphy and Jackson: A Case of Hemorrhagic Disease in the Newborn with Transfusion from the Father, Boston Med. and Surg. Jour., 1909, clxi, 407.

primary blood defect. There was no evidence of syphilis in their cases and it was inconceivable that transfusion could have immediately repaired a vascular lesion or overcome bacterial infection.

Baginski[82] is also of the opinion that there is a type of hemorrhage in the new-born for which there is no adequate explanation, and which is probably dependent on some primary blood defect or change.

It is unquestionable that there is a clinical type of spontaneous hemorrhage in new-born infants for which no definite etiologic agent has been established. From the evidence available at present, it seems only rational to suppose that the persistent hemorrhage is directly dependent on some biochemical blood defect or change. But whether an abnormality of the blood or vessels is the primary etiologic factor, or whether the hemorrhage is always secondary to some infection or disease, can only be determined by future investigation.

VI. MORTALITY

The mortality in the hemorrhagic conditions of the new-born ranges from 35 to 87 per cent. In the collected cases of Townsend[22] the mortality was 79 per cent., in those of Silvermann[6] 56 per cent. In the personal cases of Townsend the mortality was 62 per cent., in those of Lequeux[2] 87 per cent. Tarnier[83] gives the mortality as 50 per cent., and Minot[73] as 84 per cent. In cases of gastro-intestinal hemorrhage Shukowsky[10] observed a mortality of 62 per cent., while in the collected statistics of Vasmer[84] the mortality was 32.8 per cent. In cases of umbilical hemorrhage Fürth[85] observed a mortality of 100 per cent., Grandidier[16] of 83 per cent., and Hennig[86] of 68 per cent.

VII. TREATMENT

The futility of most therapeutic measures in the hemorrhagic disease of the new-born is shown by the high mortality. Recently, however, several measures have been advocated which have given more promising results.

The use of calcium salts to control the hemorrhage has been generally disappointing. Isolated cases have been reported by Doran,[87] Legge[88] and others, in which recovery has followed the use of calcium, but in the greater number of reported cases this treatment has been without effect.

Judging from the reports of continental writers, the administration of gelatin is of great value. It was first used for hemorrhage in the new-

82. Baginski: Lehrbuch der Kinderkrankheiten, Leipsic, 1905.
83. Tarnier: Quoted by Shukowsky (see note 10).
84. Vasmer: Ueber Melaena neonatorum, Arch. f. Gynäk., 1909, lxxxix, 275.
85. Fürth: Die Nabelblutung, Arch. f. Kinderh., 1884, v, 305.
86. Hennig: Gerhardt's Handbuch d. Kinderk., 1877, ii, 101.
87. Doran: A Case of Melena, Recovery, Abstr. Arch. Pediat., 1909, xxvi, 942.
88. Legge: A Case of Hemophilia Neonatorum, Brit. Med. Jour., 1908, i, 1173.

born by Guttman[89] in 1899, and favorable cases have been reported by Holtzschmidt,[9] Shukowsky,[10] Grüneberg,[90] Vasmer,[84] Torday,[91] Engelmann,[92] Schubert,[93] Heyn,[94] Sorachowitz,[95] Nohl,[14] DeBra[96] and many others. In this country Tuley[97] has observed cases in which gelatin was of value. Before the use of gelatin, Holtzschmidt[9] observed fourteen cases of hemorrhage in the new-born in which the mortality was 50 per cent. Five later patients to whom gelatin was administered, all recovered. Nohl reports six cases of gastro-enteric hemorrhage in all of which the patients recovered following the use of gelatin. He has collected statistics which show that in 244 cases of melena before the use of gelatin 113 patients died, a mortality of 46.3 per cent. He found thirty-four cases in which gelatin was used, with only two fatalities, giving a mortality of 5.5 per cent. According to Vasmer[84] the mortality in sixty-nine cases of melena was 32.8 per cent., but the thirty-seven patients treated with gelatin showed a mortality of only 8.8 per cent.

That favorable results are more often published than ones which are unfavorable, is well known, and this fact must be considered in judging the value of any therapeutic measure from collected statistics. The personal cases of Shukowsky[10] indicate that gelatin is not always as successful as the statistics of Nohl, Vasmer, De Bra, and Holtzschmidt would seem to indicate. The eleven cases with favorable termination were divided by Shukowsky into two groups, mild, and severe. In three of the mild cases the patients recovered under the use of iron sesquichlorid, and in two with the use of gelatin. In three of the six severe cases in which recovery occurred, the patients were treated with gelatin given internally and by subcutaneous injection; two were treated by means of gastric and colonic lavage, while one infant received iron sesquichlorid, ergotin, extract of krameria, musk, and cognac. Four of the patients treated with gelatin died. From these results Shukowsky concludes with Fischer that gelatin is of value, but is useless in the cases of luetic origin, or in those with hemorrhagic gastro-enteritis.

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89. Guttman: Zur Behandlung der Malaena neonatorum, Therap. Monatsch., 1899, xiii, 552.

90. Grüneberg: Zur Behandlung der hämorrhagischen Diathese beim Neugeborenen, München. Med. Wchnschr., 1908, lvi, 1, 1079.

91. Torday: Abstr. Jahrb. f. Kinderh., 1903, lvii, 104.

92. Engelmann: Abstr. Jahrb. f. Kinderh., 1910, xv, 433.

93. Schubert: Behandlung der Melaena neonatorum mit Gelatineinjectionen, Centralbl. f. Gynäk., 1907, xxxi, 201.

94. Heyn: Quoted by Schubert (see note 93).

95. Sorachowitz: Zur Behandlung der Melaena neonatorum, Abstr. Centralbl. f. Gynäk., 1907, xxxi, 1454.

96. De Bra: Die Melaena neonatorum und ihre erfolgreiche Bekämpfung durch subcutane Gelatineinjection; Inaugural Dissertation, Berlin, 1910.

97. Tuley: Hemorrhagic Disease of the New-Born, Jour. Am. Med. Assn., 1908, li, 2215.

Following the publications of Weil, animal blood sera have been used for the treatment of hemorrhage in the new-born. The published reports, however, are too meager to form any estimate of its value. Leary[98] has reported cases in which the patients recovered after the use of rabbit's blood-serum, but he has also had unsuccessful cases. Lucas[74] observed a favorable result with rabbit's serum. Swain, Murphy, and Jackson report a case in which horse and rabbit sera were ineffectual, but in which the patient was cured by transfusion of human blood.

Judging from recent publications, the most promising line of treatment at the present time is by means of human blood or its derivatives. In 1908 Lambert[80] reported a case of melena neonatorum in which the patient was treated by transfusion of human blood. The infant had hemorrhage into the skin and subcutaneous tissues, and from the nose and gastro-enteric tract. Recovery ensued immediately after transfusion. Similar cases have been reported by Swain, Murphy and Jackson,[81] Mosenthal,[99] and Newell.[100] In the cases of Schwarz and Ottenberg,[55] and Lespinasse and Fischer,[101] the transfusion was followed by marked improvement, but the hemorrhage later recurred with fatal result.

In 1910 Welch[102] reported twelve cases of hemorrhage in the new-born successfully treated by subcutaneous injection of human blood-serum. A number of the patients suffered from severe hemorrhage and the treatment was followed by immediate improvement. In a personal communication Dr. Welch informed one of us that up to that time he had treated eighteen such patients without a single fatality due to hemorrhage.

We have treated seven new-born patients with hemorrhage by means of subcutaneous injections of human blood. The first patient was treated in April, 1908, with, first, an injection of 20 c.c. of human blood-serum, and later, an injection of whole blood. The whole blood was used instead of the serum for the reason that it was easier to obtain and could be used immediately, the time required for the serum to separate being saved. It seemed an additional advantage to inject, not only the serum, but also the formed elements which have influence on the coagulation of the blood.

In most cases the blood was taken from one of the parents. The required amount was withdrawn from a vein of the forearm by means of

98. Leary: The Use of Fresh Animal Sera in Hemorrhagic Conditions, Boston Med. and Surg. Jour., 1908, iii, 73.

99. Mosenthal: Transfusion as a Cure for Melena Neonatorum, Jour. Am. Med. Assn., 1910, liv, 1613.

100. Newell: Boston Med. and Surg. Jour., 1910, clxiii, 435.

101. Lespinasse and Fischer: Hemorrhage of the Newborn; Treatment by Direct Transfusion of Blood; Review of the Literature, Report of a Case. Surg. Gyn. and Obst., 1911, xii, 40.

102. Welch: Normal Human Blood Serum as a Curative Agent in Hemophilia Neonatorum. Am. Jour. Med. Sc., 1910, cxxxix, 800.

an exploratory syringe and injected immediately into the subcutaneous tissue of the infant's back.

Of the seven infants thus treated six recovered and one died. The fatal case was in an infant who had suffered from multiple hemorrhages for eight days and died three and one-half hours after admission to the hospital. The patient was in a moribund condition when admitted and received only a single injection of 10 c.c. of blood. In five of the six cases in which recovery took place, the hemorrhage ceased soon after treatment, and at the same time there was marked improvement in the general condition. In four cases the hemorrhage was quite severe and the patients presented all of the signs of severe anemia due to loss of blood. One case was of moderate severity. In the remaining case a positive Wassermann reaction was obtained; the hemorrhage was only slightly improved after the blood injections, but ceased after the use of mercurial treatment. Whether the blood injections were of value in this case is difficult to determine.

The subcutaneous injection of whole blood is not without hypothetic objection. The formed elements possibly act as foreign material and must be broken up and excreted. From clinical experience with the method we have found this objection of no obvious importance. In every case the blood was entirely absorbed within a few hours and, so far as could be determined, had no bad influence on the patient's general condition.

It is always hazardous to draw conclusions from small series of cases, and this danger is very real in reference to the treatment of the hemorrhagic conditions of the new-born. The hemorrhages are of varying severity and are due to different causes. Probably some of the cases recover spontaneously, and this is indicated by the number of therapeutic measures which have given favorable results in isolated cases. The true value of any therapeutic agent can be judged only by a large series of cases.

It seems, however, that the best results can be expected from the use of human blood or serum. In the four successful cases the curative effect of blood transfusion was immediate, but this method of treatment must have a rather restricted field. The technical difficulties of transfusion in a young infant are formidable and render the method available only in the hands of a very skilful surgeon.

The value of blood-serum is shown by the results obtained by Welch, and its use is free from the hypothetic objection which applies to the use of whole blood. On the other hand, if the immediate cause of the hemorrhage is the absence of any of the elements essential to blood-coagulation, the use of whole blood would appear to be a more rational procedure. Moreover, the technic is simpler; the whole blood can be used immediately, and in our experience has been efficacious and without apparent harm.

REPORT OF CASES[103]

CASE 1.—The family history was unimportant. The patient, a female infant, was born at the Nursery and Child's Hospital April 13, 1908. The labor was normal. The birth-weight was six pounds.

There was nothing abnormal until April 15, on which day the morning temperature (rectal) was 101 F.; the baby was restless, cried considerably, and made no attempt to nurse. The temperature at 6 p. m. was 102 F. At 8 p. m. about 20 c.c. of blood was expelled from the bowels. Shortly after the hemorrhage, 5 gr. calcium lactate was given by subcutaneous injection, and the same quantity given by mouth every hour for three doses. At 11 p. m. there was a second rectal hemorrhage and at 11:30 a third. A small amount of blood was also vomited. At this time the patient was quite pallid, the skin was dry and wrinkled and the cry very feeble. The rectal temperature was 96 F., the pulse was weak and too rapid to be counted accurately. A fourth hemorrhage occurred at 12 p. m.

At 12:15 a. m., April 16, 20 c.c. of blood-serum from the mother was injected into the subcutaneous tissue of the infant's back. Two hours later a small, slightly blood-tinged stool was passed. It was impossible to judge whether this blood represented a fresh hemorrhage or was the remains of the previous ones. An injection of 10 c.c. of the mother's blood was given at this time. April 16,

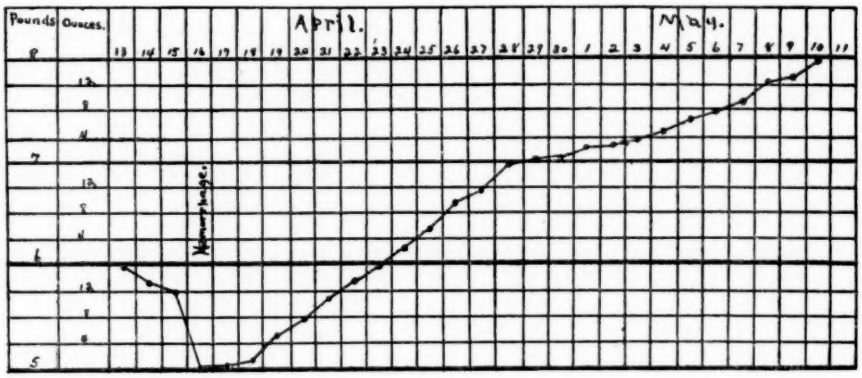

Chart showing weight curve in Case 1, Baby B, breast-fed, having hemorrhages on the fourth day. Treatment by injection of the mother's blood.

the morning temperature was 102 F.; the evening temperature 101. There were no further hemorrhages.

From this time—as shown by the weight chart—the recovery was uneventful. The blood given in the second injection had disappeared entirely by the following morning. April 18, the blood coagulated in four minutes.

Shortly after the first hemorrhage, a deep puncture was made in the lobe of the infant's ear, from which there was a steady oozing of blood. About 1 c.c. of blood was received into a glass tube with drawn out ends and was used to inoculate broth, agar, and blood-serum. The media showed no bacterial growth after incubation at 37 C. for two days.

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103. Case 1 was from the service of Dr. C. F. Collins at the Nursery and Child's Hospital. We desire to express our thanks for the privilege of using the history. We are indebted to the late Dr. J. H. McInerny for the opportunity of observing Case 2 and to Dr. Donald MacNaughton for the privilege of reporting Case 9. The remaining cases were from the service of Drs. Judd and Commiskey at the Kings County Hospital in Brooklyn. The blood examinations in these cases were made by Dr. C. Schradeick, resident pathologist at the Kings County Hospital, to whom we wish to express our thanks.

About 1.5 c.c. of blood was collected in a small test tube and at the end of one and one-half hours there was no evidence of coagulation. Two drops of a 1 per cent. solution of calcium chlorid solution, when added to a few drops of the infant's blood, did not cause clotting. The further addition of calcium chlorid was without effect. The remaining blood was divided into two portions, to one of which was added a few drops of defibrinated blood from the mother. A firm clot formed in three to four minutes.

To the second portion of the infant's blood was added a few drops of defibrinated blood which had been heated for thirty-five minutes at from 60 to 63 C. A loose meshed clot was formed in six to seven minutes. The coagulation time of the mother's blood was three and one-half minutes.

This patient was seen October 4, 1910, and at that time weighed thirty-one pounds. There had been no history of bleeding and the blood coagulated in three and one-half minutes. A positive Wassermann reaction was obtained from the blood of both the mother and the child. The mother denied having any manifestation of syphilis. The child had been in good health, with the exception of a persistent nasal discharge at the age of 20 months. The physical examination showed a rather suggestive depression in the bridge of the nose but other stigmata of lues were not observed.

CASE 2.—A male infant, born Jan. 27, 1909, after a normal labor, and weighed eight and one-half pounds at birth. The family history was negative.

Soon after birth a swelling was noted in the occipital region of the skull. The mass was about 5 cm. in diameter; the contents were fluid. On the second day of life the mass had increased to nearly twice its previous size. The baby nursed well, was without fever, and when seen in the forenoon showed nothing abnormal except the hematoma.

January 30, at 6 p. m., a moderate amount of blood was expelled from the rectum and a second smaller hemorrhage occurred during the night. In the forenoon of the next day, January 31, the infant passed two bloody stools and vomited a small amount of blood-stained material. The temperature at this time was 98 F. (rectal) and all feedings were refused. The hematoma seemed about the same size as on the previous day.

At 3 p. m. January 31, 20 c.c. of the father's blood was injected into the infant's back. One-half hour later the baby vomited a small amount of blood-streaked material. A second injection of 10 c.c. of blood was given at 7 p. m. There was no further bleeding. The feedings were taken well and at the end of two weeks the baby appeared to be normal for its age.

January 31, about 1 c.c. of blood was obtained from the baby by means of a lancet-puncture in the heel. After standing for one-half hour the blood showed a few fibrin flocculi but no definite clot was formed. The experiments described under Case 1 were made, with the same results.

After recovery the infant's blood coagulated in from three to four minutes.

CASE 3.—The patient, a male infant, was born at the Kings County Hospital, Dec. 3, 1909. The family history was irrelevant. The head had been born in an occipitoposterior position; at birth the face was edematous, and on each eyelid near the inner canthus was an excoriated area about 1 cm. in diameter. About twenty-four hours after birth blood began to ooze from these areas. Pressure and the application of adrenalin solution did not control the hemorrhage. Ten c.c. of blood from the mother was injected into the subcutaneous tissue of the infant's back. The hemorrhage continued, with perhaps slightly lessened intensity, but in twenty-four hours had resumed its former severity. A second injection of 10 c.c. of blood was given. Twelve hours later the coagulation-time was nine minutes and the hemorrhage had not ceased. A Wassermann reaction was positive and on this basis inunctions of mercurial ointment were given.

The bleeding began to decrease, and twenty-four hours later had entirely ceased. The infant was discharged in good condition when 14 days old. There was no fever during the hemorrhage and general signs and symptoms were

absent. Three days after the cessation of hemorrhage the blood coagulated in eight and one-half minutes.

CASE 4.—The family history contained nothing of importance. The patient, a female infant, was born at the Kings County Hospital August 28, 1910.

August 30 there was a rather profuse intestinal hemorrhage. During the next twelve hours blood continued to escape from the rectum at intervals and the infant became pale, the face was drawn, and the pulse rapid and weak. Ten c.c. of blood from the mother was injected in the usual manner. At this time the infant's blood coagulated in five and one-half minutes and there was continuous bleeding from the puncture from which the blood was obtained. The bleeding diminished after the blood-injection and had entirely ceased twelve hours later. There were no further intestinal hemorrhages.

After recovery the blood coagulated in seven minutes and there was no continued bleeding from the wound from which the blood was obtained for clinical examination. During the hemorrhage, the temperature was not above normal, and was subnormal (97 F. per rectum) at the time the blood was injected.

CASE 5.—A male infant, born in the Kings County Hospital August 26, 1910. On the day of birth it was noted that there was swelling of the eyelids and that there was a slight oozing of blood from the conjunctiva. August 28, the infant vomited about ½ ounce of bright red blood. During the course of the next twelve hours blood was vomited on three separate occasions. A puncture wound in the lobe of the right ear from which blood was taken for clinical examination gave rise to continuous bleeding. The infant became pale, was feeble, and showed the effect of the loss of blood. Five c.c. of blood from the mother was given in the usual way. There was no further hematemesis. The bleeding from the conjunctiva lessened, but twelve hours later there was still a slight oozing of blood from this source and from the wound in the ear. At this time 10 c.c. of blood, from a healthy antepartum patient in the seventh month of pregnancy, was given.

The hemorrhage ceased within a short time after the last blood injection and did not recur.

During the hemorrhage (before the first blood injection) the coagulation-time was nine minutes; after recovery it was three and three-fourths minutes. The infant's blood gave a negative Wassermann reaction.

CASE 6.—A female infant, 8 days old, was admitted to the Kings County Hospital Sept. 15, 1910. The family history was unimportant.

Shortly after birth there was oozing of blood from the stump of the umbilical cord. Two days later the baby became jaundiced and a few ecchymoses were noted on the right shoulder, the right hand and on the abdomen in the region of the umbilicus. On the sixth day there was a profuse umbilical hemorrhage. The patient was extremely weak.

Adrenalin, gauze pressure, suture, etc., were ineffective in controlling the hemorrhage. On the seventh day there was another profuse hemorrhage from the cord.

At the time of admission the baby was intensely jaundiced, and ecchymotic spots were on the shoulder, abdomen, and right hand. There was continuous oozing of blood from the abdominal end of the umbilical cord. One and a half hours after admission the coagulation-time of the blood was three and one-half minutes. An injection of 10 c.c. of the mother's blood was given at this time. The rectal temperature at the time of admission was 97 F.

Three and a half hours after admission the infant died. Permission for post-mortem examination was refused.

CASE 7.—A male infant, born at the Kings County Hospital Jan. 17, 1911, at 8:20 p. m.

The family history was unimportant. The labor was uneventful; the baby was apparently normal and weighed seven pounds and one ounce at birth.

January 18, about 6 p. m., blood began to ooze from the conjunctiva and the nasal mucous membrane. A small amount of blood was also vomited. The

hemorrhage was slight and ceased spontaneously. Physical examination at this time was negative.

In the forenoon of January 19 there was a reappearance of the conjunctival hemorrhage and there was profuse bleeding from the umbilical cord at its junction with the abdominal wall. The umbilical hemorrhage was checked by local application of 1-1000 adrenalin solution.

At 6 p. m. there was a slight hemorrhage from the umbilicus, which ceased after the use of adrenalin solution.

A profuse umbilical hemorrhage occurred at 10:30 p. m. After using various local measures with no success the umbilical hemorrhage was finally controlled by the application of continuous ligatures over the whole umbilical stump. The hemorrhage from the conjunctiva reappeared and blood was noted in the stools. At this time the infant was pallid and feeble and showed the effect of the repeated hemorrhages.

January 20, 5 c.c. of blood was withdrawn from the median basilic vein of the mother and injected into the muscles of the infant's back.

There was no further hemorrhage and the infant began to improve. January 24, the infant was in good condition and was discharged from the maternity ward. There was no fever during the illness; the highest temperature was 100 F. (rectal).

Coagulation-time of the blood: January 20, six minutes; January 21, five minutes; January 22, one and one-half minutes.

CASE 8.—A full term male infant, born at the Kings County Hospital on Sept. 12, 1910. The birth-weight was five pounds and twelve ounces and the infant was apparently normal. The family history was unimportant.

During the first seven days the baby gained weight and was apparently healthy. On the eighth day the infant refused to take the breast and was fed from a spoon. On the day following, while being fed, the baby suddenly became extremely cyanotic. The pulse was feeble and too rapid to be counted. Death ensued within fifteen minutes.

On post-mortem examination the heart was found congested and both auricles were filled with dark, fluid blood. The lungs were hyperemic and showed scattered areas of atelectasis. Beneath the capsule of the liver there were three or four ecchymoses 2 to 3 cm. in diameter, and small hemorrhages were present throughout the liver substance. The whole organ was extremely congested.

The kidneys were very hyperemic. The brain, spleen, pancreas, suprarenals and thymus were anemic, but were otherwise normal.

The blood throughout the body was dark and showed no evidence of coagulation.

Sections of the liver were stained by the Levaditi method but no spirochetes could be found.

CASE 9.—A male infant, born at the Samaritan Hospital June 9, 1910. The birth-weight was ten pounds.

Nothing abnormal was noted until the seventh day, at which time the baby nursed poorly and vomited several feedings. The vomiting continued, the stools were green and loose, and the temperature ranged from 99 to 106 F. Physical examination disclosed nothing abnormal. On the twelfth day the urine was slightly blood-stained.

The infant died on the thirteenth day without showing any definite signs beyond those already noted.

At the post-mortem examination the mucous membrane of the intestines was moderately congested. With the exception of the right kidney and suprarenal gland the remaining organs showed nothing of importance.

The right kidney and suprarenal were three times the normal size. The suprarenal was practically converted into a blood-cyst by parenchymatous hemorrhage. The pelvis of the kidney was filled with blood and the parenchyma was greatly distended by multiple hemorrhages.

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INFLAMMATORY CHANGES IN THE APPENDIX DURING EARLY INFANCY *

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The following report of an investigation of inflammatory changes in the appendix during early infancy is made from the autopsy findings in 200 consecutive cases at the New York Foundling Hospital, from January to September, 1910. The patients selected were the youngest possible, and comparatively few exceeded three months in age.

Ribbert[1] found that obliterative changes in the appendix, regarded by him as a process of physiologic involution, occurred during the first decade in 4 per cent. of cases. MacCarty,[2] in an extensive study of the material of the Rochester, Minn., clinic, found that partial obliteration of the lumen of the appendix might be present as early as the fifth year, and complete obliteration was seen as early as the tenth year. He estimates that the average time necessary for complete obliteration of the lumen of the appendix is approximately four years, and believes that pathologic processes must determine these rapid changes.

It has long been known that the frequency of appendicitis, seen clinically, increases from infancy through the years of childhood to puberty. Deaver[3] has found that the frequency of appendicitis occurring during the first five years of life is about 8 per cent. A good many cases of appendicitis occurring during infancy are now on record, and these are reported most frequently in infants during the latter months of the first year or during the second year. A few rarer instances of appendicitis are reported as occurring as early as the fifth or sixth week. Gastro-intestinal symptoms of varying severity have frequently preceded these attacks. Deiss,[4] in 1908, reported a case of appendicitis with peritonitis in a child of two weeks. The lesion was found at autopsy, the child exhibiting clinically acute gastro-intestinal symptoms for eight days preceding its death.

The clinical course in the hospital of these infants dying early of malnutrition offers but little of note. A few had been born in the hospital in the obstetrical service, and then transferred to the children's ward. In great part they had been admitted to the institution several

* From the Department of Pathology of Washington University.

1. Ribbert: Virchow's Arch. f. path. Anat., cxxxii, 66.
2. MacCarty: Jour. Am. Med. Ass'n., lv, 488.
3. Deaver: Jour. Am. Med. Ass'n, lv, 2198.
4. Deiss: Basle Dissertations, 1908, p. 63.

days after birth, many coming from the city maternity hospitals. Some had been breast-fed, but the majority had been artificially fed from the start. Breast feeding, but more often artificial feeding with some modification of milk, was continued after the child entered the hospital service. On admission these children were in a weak, anemic, often emaciated condition, with all the chief symptoms referable to the gastro-intestinal tract. Temporary improvement was at times seen, but the usual course was a progressive loss of weight, with increasing intestinal disturbance, death occurring quickly in this state of malnutrition.

It is well known that infants dying with severe gastro-intestinal symptoms will often, at autopsy, show only slight anatomic changes. R. Fischl[5] has recently reviewed these histologic changes of the gastro-intestinal tract in acute and chronic diseases of malnutrition. The stomach is found practically normal. At times the cells in the glands of the stomach undergo a peculiar swelling suggesting a coagulation necrosis. Fischl has found hypertrophic changes in the crypts of Lieberkühn with occasional formation of small cysts. In the more acute cases, the hyperemia of the small intestine in different areas is very marked, and small hemorrhages occur in the mucosa. Near the hemorrhages superficial necrosis of the epithelium is often found. Fischl has pointed out that at times the epithelium appears swollen, with poorly staining nuclei, suggesting an effect which a poison might produce when acting on the cells. The follicles of the large intestine are frequently prominent and surrounded by a zone of hyperemia. In the region of the follicles small ulcers may appear and these are usually of superficial character. Peyer's patches are but little involved. A well-marked hyperemia and a hyperplasia of the mesenteric lymph-nodes has been noted.

A belief that the appendix might offer a point of least resistance to infection of the gastro-intestinal tract, and the hope of finding some etiologic factor explaining the peritoneal exudate found to be present occasionally in such young infants at death, led to a systematic histologic examination of a series of appendices. The material was obtained soon after death, the time varying from a few minutes to twenty-four hours. The appendix and a part of the wall of the cecal region in each case were preserved in formaldehyd solution and the sections cut in paraffin.

Among 200 appendices examined, fifteen showed inflammatory changes of varying intensity. A brief report of these cases follows.

CASE REPORTS

CASE 1.—Autopsy 815. R. D., male aged 1 month, 15 days; length of body 53 cm.

Anatomic Examination.—On opening the abdomen the intestines are found considerably distended, injected and matted together by thick yellowish pus. The

5. Fischl, R.: In Pfaundler and Schlossman, Disease of Children, iii.

greatest collections of purulent matter seems to be in the lower abdomen. In places the adhesions are very dense, especially in the region of the cecum, and when this is lifted from the posterior parietes, a small abscess containing thick green pus is entered. The greater part of the appendix has been destroyed. A small ragged portion of the base measuring about .5 cm. arises from the posterior surface of the cecum. A small piece of necrotic tissue (later identified microscopically as appendix tissue) lies in the upper part of abscess cavity, hanging loosely to the posterior surface of the colon. The mucosa of the large intestine is intensely congested; it contains many small superficial ulcers in the site of the follicles of the cecal region, of the hepatic flexure and of the sigmoid. No ulcer has caused perforation. The small intestine in places is a good deal congested, but has no ulceration. The stomach, liver, spleen, kidneys, lungs and heart seem normal. Smears from the exudate of the peritoneum show the presence of pus and streptococci.

Microscopic Examination.—A section has been taken through the base of the appendix. The mucous membrane is destroyed; there is intense infiltration of muscularis and serosa, with polynuclear leukocytes and lymphocytes. A similar inflammation is found in the portion representing the remains of the tip of the appendix found in the abscess cavity adherent to the colon. Sections through the ulcers of the large intestine show that these are small and superficial. Sections of the other viscera are normal. Liver sections stained for *Spirochæte pallida* are negative.

Case 2.—Autopsy 812. M. O., female, aged 24 days; length of body 49 cm.; weight 5 pounds. Autopsy confined to abdomen and thorax.

Anatomic Examination.—On opening the abdomen the intestinal coils are slightly distended, considerably injected and loosely glued to one another by a thin, yellowish exudate. This exudate is greatest in amount in the lower abdomen, especially on the right side. The cecum is found in the iliac fossa loosely bound to the abdominal wall by yellow exudate. The appendix, measuring 4.5 cm., hangs over the pelvic brim. It is swollen and dark red; the tip is almost black in color, but shows no perforation. The pelvic organs are all deeply congested, and the right tube is dark red in color. The liver, kidneys and spleen are normal in size and form. The thoracic viscera are apparently normal, save that the lungs are hyperemic, especially at the bases. The large intestine has areas where the mucous membrane shows deep congestion, with marked prominence of the follicles. On gross examination no ulcerations are found. There is deep congestion of the mucosa of the small intestine in places. Smears from the peritoneal exudate show the presence of pus cells and staphylococci.

Microscopic Examination.—The appendix was sectioned in a number of places; the mucosa of the tip is almost entirely destroyed. The muscle-coats and serosa are edematous and intensely infiltrated with polynuclear leukocytes and lymphocytes. Lymph-vessels and veins are distended with leukocytes. There is thrombosis of a medium sized artery in the mesentery close to the outer muscle-coat. The tissue nearest the mesentery is best preserved, while that opposite the mesenteric border is almost entirely necrotic. In sections made near the base, the inflammation is much less marked. The cecum near the origin of the appendix shows the serosa alone involved. Sections made through the uterus and both Fallopian tubes present a normal mucosa and muscularis, but the serosa is very edematous and densely infiltrated with inflammatory cells. The other viscera are practically normal. *Spirochæte pallida* could not be demonstrated in the liver.

Case 3.—Autopsy 1007. H. J., male, aged 17 days.

Anatomic Examination.—The body is that of a poorly nourished infant 46 cm. in length. The skin is slightly jaundiced having a light yellowish color. Examination is confined to abdomen and chest. On opening the abdomen the intestines appear congested and are bound together loosely by what appears to be a thin

fibrinous exudate, confined mostly to the lower right side. The cecum is found in the iliac fossa fixed well forward, close to the anterior abdominal wall; its presenting lower margin is adherent to the peritoneum covering the iliac fossa by flakes of fibrin. The appendix passes inward and to the left over the psoas down into the pelvis. It is much swollen, deep, dark red, especially near the tip, and is adherent to the brim of the pelvis in its inner third and adherent to the sigmoid in its outer two-thirds, the sigmoid being a large loop extending to the right beyond the mid-line of the body. The mesentery of the appendix shares in these loose adhesions. The adjacent lymph-glands seem moderately swollen and larger than the mesenteric glands elsewhere.

Examination of the appendix shows that it is 5 cm. long. The walls appear thickened and the mucous membrane dark red; the lumen contains a brownish red substance. In the smears taken from the peritoneal cavity are pus cells and Gram-negative bacilli suggesting the colon type. The mucous membrane of the stomach, the lower part of the small intestine and the entire large intestine are distinctly congested. The lymph-follicles of the large intestine are quite prominent and surrounded by a reddened zone; apparently nowhere is there ulceration that can be appreciated on gross examination. The gall-bladder has a normal appearance and is filled with thick, dark bile. The hepatic and common bile ducts are patent.

Microscopic Examination.—The sections are made through the appendix and the sigmoid at the point of maximum adhesion. The sigmoid appears quite normal, save that the serosa is very edematous and shows the presence of many leukocytes and lymphoid cells. In contrast with the appearance of the sigmoid, the wall of the appendix is uniformly, in some places very densely, infiltrated with inflammatory cells. Sections made from other parts of the intestine and other viscera present nothing unusual, save that the kidneys show a moderate parenchymatous degeneration.

CASE 4.—Autopsy 900. H. H., male, aged 27 days; length of body 51 cm.

Anatomic Examination.—The cecum is in the iliac fossa, and the fixation of the colon occurs below the iliac crest. The appendix measures 3.5 cm. in length, and arises posteriorly. The first part of the appendix lies in an erect position behind the cecum and the ascending colon. As it meets the reflection of the peritoneum from the colon to the iliac fossa, a sharp bend occurs directing the tip of the appendix downward and inward. The entire appendix is fixed to the cecum and the iliac fossa, save a small part of the tip, which remains free. At the bend in the appendix there is a good deal of redness and edema.

Microscopic Examination.—The mucosa and the submucosa opposite the mesenteric border are necrotic, but in other parts are fairly well preserved. There is intense infiltration of the muscularis and the serosa everywhere. There is a thrombosis of one of the larger arteries in the wall of the appendix near the mesentery which has resulted in partial occlusion of the vessel.

CASE 5.—Autopsy 890. E. C., female, aged 24 days; length of body 50 cm.

Anatomic Examination.—The cecum is found in the iliac fossa and the proximal part of the ascending colon is fixed to the iliac fossa at a point below the iliac crest. The appendix, 4 cm. in length, passes up and inward, the distal part lying behind the terminal coil of the ileum. The appendix looks moderately swollen and congested, and is covered in places by a few small flakes of yellowish fibrin.

Microscopic Examination.—The mucosa is well preserved and the lumen contains many pus-cells, a moderate number of red blood-cells and bacteria,. The muscularis and serosa are moderately swollen and show the presence of a fair number of leukocytes scattered here and there. The sections through the wall of the cecum are normal.

CASE 6.—Autopsy 1015. V. R., male, aged 24 days; length of body 48 cm.

Anatomic Examination.—The body is that of an emaciated infant 50.5 cm. long; weight about 4 pounds. Examination confined to abdomen and chest. On opening the abdominal cavity, the small intestine is very moderately distended. The cecum is in the iliac fossa; the proximal ascending colon is fixed to the iliac crest by a small mesocolon. The appendix 4 cm. in length, passes upward and to the left so that the tip lies behind the terminal coil of the ileum. It is bent on itself near the middle, and appears red and moderately swollen. On splitting open the appendix the walls seem thickened; the mucous membrane appears dark red in color. The lumen contains a reddish brown fecal matter. The adjacent cecum shows also a congested mucous membrane, but it has not as deep a color as the appendix. The lymph-follicles of the large intestine stand out prominently, but without evidence of ulceration. The small intestine and the stomach are of normal appearance.

Microscopic Examination.—The inflammatory changes in the appendix are of slight character. There is a moderate infiltration with inflammatory cells of the muscular coat and the peritoneum, especially in the region of the mesentery. The cecum is normal.

CASE 7.—Autopsy 912. H. L., female, aged 1 month, 5 days.

Anatomic Examination.—The cecum is in the iliac fossa and the proximal part of the ascending colon is fixed to the posterior parietes, above the level of the iliac crest. The ascending colon has no mesentery. The appendix, measuring 4 cm. in length, extends straight upward behind the first part of the ascending colon, but is not adherent to either. It has no deflections. It appears slightly reddened and swollen.

Microscopic Examination.—The mucosa is well preserved and shows but little change. Submucosa, muscularis, and the serosa are infiltrated with a considerable number of leukocytes, lymphocytes, and eosinophil cells. The section of the cecum presents a small area in the muscularis with a similar infiltration, but this is not very extensive.

CASE 8.—Autopsy 888. V. Y., male, aged 30 days; length of body 49.5 cm.; weight 5 pounds.

Anatomic Examination.—The cecum is found in the iliac fossa; the colon is fixed to the iliac crest without a mesentery. The appendix arises posteriorly and lies directly behind the cecum and the first part of the ascending colon. It measures 4.5 cm. in length and is bent on itself near its mid-point so that the distal part lies parallel to the proximal part. The entire appendix seems swollen and injected and is covered with a fine yellowish exudate. Smears made from the exudate contained pus-cells, degenerated epithelial cells, a few streptococci and many Gram-negative bacilli. Cultures contained *B. pyocyaneus.*

Microscopic Examination.—The mucosa of the appendix is poorly preserved because of autolytic changes. The muscularis and the serosa are infiltrated with many leukocytes and lymphocytes. Sections made through adjacent lymph-glands exhibit the microscopic evidence of acute inflammation.

CASE 9.—Autopsy 841. E. P., female, aged 23 days; length of body 48 cm.

Anatomic Examination.—The cecum lies in the iliac fossa. The appendix arises from the cecum in the usual manner, passing upward behind the terminal part of the ileum. It has a sharp bend downward near its mid-point. It measures 4 cm. and appears swollen; the tip is reddened and adherent to the cecum and iliac fossa by a loose, fine, yellowish exudate.

Microscopic Examination.—The mucosa is fairly well preserved. The muscle-coats are moderately swollen and show a marked infiltration with polynuclear leukocytes, lymphocytes and eosinophils. The serosa, in which the vessels are greatly engorged, has an infiltration similar to that of the muscularis. There is thrombosis of one of the smaller arteries of the mesentery. Sections from the

wall of the cecum are normal, save for considerable swelling of the serosa, and in places moderate infiltration with polynuclear leukocytes and lymphocytes.

CASE 10.—Autopsy 929. M. G., female, aged 1 month, 3 days; length, 50 cm.

Anatomic Examination.—The cecum is found in the iliac fossa; the proximal colon begins to be fixed to the posterior parietes above the iliac crests at the lower pole of the right kidney. The appendix here again arises posteriorly, and passes directly upward to the lower pole of the right kidney where it becomes bent down and inward. The tip alone is adherent, the adhesion being with the posterior parietal peritoneum. The entire appendix, which measures about 5 cm., seems deeply congested, but especially so in the distal portion.

Microscopic Examination.—The lumen of the appendix appears considerably distended. There is great hyperemia of all the blood-vessels. The mucous membrane contains many polynuclear leukocytes, lymphocytes and eosinophils, and besides has small hemorrhages. The muscle coats are rather thin. The serosa is very swollen and edematous. Considerable numbers of leukocytes and eosinophil cells are found everywhere. The cecum is normal.

CASE 11.—Autopsy 1037. J. S., male, aged 29 days; length of body, 51 cm.

Anatomic Examination.—The cecum lies in the iliac fossa. The appendix arises posteriorly; its proximal part ascends in close relation with the cecum and the ascending colon. Where it meets the reflection of the peritoneum from the colon to the iliac fossa, which occurs below the crest, it is bent on itself like a fish-hook. It appears dark red in color and swollen, especially in the distal part.

Microscopic Examination.—The mucosa in the distal portion of the appendix is poorly preserved. The edematous muscularis and serosa contain many leukocytes. Sections from the proximal part of the appendix are practically free from inflammatory changes. The cecum is normal.

CASE 12.—Autopsy 848. D. L., male, aged 28 days; length of body, 51 cm.

Anatomic Examination.—The cecum is found in the iliac fossa. The proximal part of the ascending colon, having no mesentery, is fixed just below the iliac crest. The cecum turns back sharply and gives rise to the appendix, which lies in an erect position directly behind the cecum and the ascending colon, to both of which it is closely adherent. The tip of the appendix is bent sharply downward, the deflection occurring evidently where the appendix meets the line of fixation of the ascending colon to the iliac fossa. The tip of the appendix is slightly swollen, but very much reddened. The appendix measures 4 cm. in length.

Microscopic Examination.—Nearly the entire mucosa and the submucosa appear granular and necrotic. A small wedge-shaped segment survives and is bounded by a necrotic margin on each side. This small area exhibits marked hyperemia, and contains some extravasation of red-blood-cells. The muscular coat and the serosa are intensely infiltrated with inflammatory cells. This section suggests an infarction with a marked secondary inflammation. The cecum is normal.

CASE 13.—Autopsy 937. D. E., female, aged 13 days; length of body 47 cm.; weight 4¼ pounds.

Anatomic Examination.—The cecum is in the iliac fossa, well anteriorly, near the abdominal wall. The ascending colon is fixed in the iliac fossa by a short mesentery. The proximal part of the appendix passes over the psoas muscle; the distal portion lies over the brim in the pelvis. There are no adhesions, but a small amount of fibrin covers a slightly swollen and reddened surface. On opening the appendix, the mucous membrane appears of a red color, and the lumen contains a small amount of yellow fecal matter.

Microscopic Examination.—Small areas of hemorrhage are found in the mucosa, which is very hyperemic. The vessels of the mesentery are distended with blood. In one artery are many leukocytes lying in close contact with the intima. The mesentery and the serosa contain a considerable number of leukocytes and

lymphocytes. The muscularis is very thin and shows only a few inflammatory cells. Sections of the cecum are normal.

CASE 14.—Autopsy 953. M. K., aged 27 days; length of body 50 cm.

Anatomic Examination.—The cecum is undescended and lies above the crest of the ilium, fixed there by irregular adhesions to the posterior parietes and to the lower pole of the right kidney. The appendix lies behind the cecum and the ascending colon and is embedded in the adhesions as far as the tip, which still remains free. The tip of the appendix touches the under surface of the liver and is deflected outward at an angle of about sixty degrees. On gross examination no pathologic changes are apparent.

Microscopic Examination.—A small thrombus in an artery with partial occlusion of the lumen occurs in the outer part of the muscularis. Inflammatory cells in considerable numbers are scattered here and there throughout the section. Sections of the cecum are normal.

CASE 15.—Autopsy 989. M. B., aged 1 month and 22 days; length of body 52 cm.

Anatomic Examination.—The cecum is undescended and lies above the iliac crest below the liver. The appendix hangs vertically downward and measures 4 cm. The mesentery of the appendix is formed by the anterior vascular fold instead of the posterior. The tip of the appendix is congested, but the base has a normal color.

Microscopic Examination.—The tip of the appendix has a good deal of infiltration of its wall with polynuclear leukocytes and lymphocytes. In contrast with this, the sections made through the base exhibit merely mild inflammatory changes.

In the cases above reported, inflammatory changes occurred in the male seven times, in the female eight times. The two youngest infants were 13 days and 17 days old, respectively. In nine instances, the age ranged between 20 and 30 days. Four cases were between a month and two months old.

A reference is made in each protocol to the anatomic relations of the cecum and the appendix. In two instances (Cases 14 and 15) the cecum was still in an incompletely descended position, lying between the iliac crest and the liver; but in the remainder of the cases the cecum occupied its usual position in the iliac fossa. Three times the distal part of the appendix was found hanging over the pelvic brim, and in such instances the distal part gave the evidence of severe inflammation. In eight cases the appendix occupied a position directly behind the cecum and proximal part of the ascending colon. It is in this position of the appendix that in infants sharp angulation frequently occurs. The cause apparently is found in the relatively small retrocolic compartment at the time of birth, to which a relatively large appendix accommodates itself. Thus, the appendix passing upward directly behind the cecum and colon, may be bent sharply downward by the upper limit of the retrocolic space formed by the reflection of the peritoneum from the ascending colon to the iliac fossa or posterior parietes. Under normal conditions, even, fusion of the appendix with the cecum, ascending colon, posterior parietal peritoneum or iliac fossa is frequently found. There may result from these condi-

tions not only a permanent fixation of the sharply bent appendix, but also changes in the form of the mesentery of the appendix, possibly causing circulatory disturbances. In the majority of the cases reported above, inflammation occurred when the appendix was found sharply bent on itself, lying in close relation with the cecum and colon; and in several instances the inflammation was more marked at the site of angulation than in other parts of the appendix. In three cases, the proximal part of the appendix passed upward, inward and to the left, so that the distal part lay curled behind the mesentery of the terminal coil of the ileum. The last described position of the appendix is that most frequently found in infants, as it formed 50 per cent. of all cases in 1,050 autopsies in infants studied by me. It is of interest to note that although the majority of inflammatory changes were found in appendices lying erect directly behind the cecum and colon, this variation in position of the appendix in the infant was found in only about 25 per cent. of all infants. Sharp angulation of the appendix leading to obstruction of the lumen, causing retention of contents in the distal portion of the appendix, may be regarded as a factor influencing the inflammatory changes. Heile[6] has studied the very rapid destruction of the epithelium and other elements of the intestinal wall experimentally, and believes that these changes are due to bacterial toxins and other chemical poisons elaborated in the decomposition of fecal matter which takes place when obstruction of the lumen has been produced.

The peritoneal exudate found in seven of the cases varied considerably in amount and character. With slight inflammatory changes in the appendix, a light yellowish exudate covered the reddened surface of the appendix and glued it to the adjacent peritoneum. In the severer cases, the picture did not differ from that seen in the adult when a spreading peritonitis occurs. The smears and cultures made from the exudate showed in one case staphylococci, in a second streptococci, and in a third there were bacilli of the colon type. In one instance, the cultures were rapidly overgrown with *Bacillus pyocyaneus*. I have found a similar peritoneal exudate five times in 800 previous autopsies in infants. No histologic examination had been made of the appendix in these instances.

The gross appearance of the appendix in all cases save one, gave evidence of considerable swelling, and of redness that varied from a pinkish color in mild cases occurring merely at the point of maximum inflammation, to the dark reddish brown color seen in the severer forms of inflammation associated with the peritonitis. The mucous membrane in mild cases looked hyperemic, and occasional small reddish petechial spots were found. In severe instances the inner surface appeared dark red and the lumen was filled with a reddish-brown necrotic material. Fecal material was found not infrequently in these appendices, but apparently

6. Heile: Mit. a. d. Grenzgeb. d. Med. u. Chir., xxii, Part 1.

not in the firm masses so commonly seen as enteroliths in inflamed appendices in older children and in the adult. No parasites were found in the lumen on gross or microscopic inspection of the contents of the appendix.

The histologic changes have considerable interest and are of as advanced nature as those often seen in adult inflammatory conditions, when the process is of an acute suppurative character. Aschoff[7] a short time ago, and Obendorfer[8] still more recently, have reviewed the histology of the appendix in the new-born and in infancy. Aschoff finds that the lymphatic tissue in the mucosa and in the submucosa is relatively poorly developed at the time of birth. A rapid increase in the lymphatic elements occurs soon after birth and continues steadily until the latter years of childhood, when a decrease of lymphatic tissue gradually takes place. He shows that lymphocytes, "larger lymphoblastic" cells, mast cells and eosinophils are present at the time of birth, but that plasma cells make their appearance only after birth. The surface epithelium at first consists almost entirely of goblet cells, but these decrease in number very soon after birth. The muscle coats in the appendix of the new-born are thin and at times show some irregularities in the density of the muscle bundles. With the general increase of the lymphatic tissue in the mucosa and in the submucosa, groups of lymphocytes are frequently found here and there in the muscularis and serosa and produce an appearance which may simulate inflammation. Aschoff finally points out that the folds in the mucous membrane in the infant's appendix are not as distinct as in later life; the presence of the folds, he thinks, is of importance in the genesis of inflammation.

The earliest changes with inflammation of the appendix are difficult to recognize even in the adult, and could not always be satisfactorily studied in this series of autopsies. Autolytic changes were so rapid in onset, that even in several cases in which the autopsy was done immediately after death, with the body warm, autolysis had begun in the appendix, although the mucosa was well preserved in other parts of the intestine. Even in cases of mild inflammation, the hyperemia is very striking. Areas of extravasation of red blood-cells occur frequently in the mucosa. The occurrence of pigment has not infrequently been described even in the infant appendix. Hyperemia and small hemorrhages were naturally most marked in instances in which thrombosis was found in some of the arteries in either the wall of the appendix or the mesentery. When thrombosis was present, the mucosa and submucosa in places histologically suggested the picture of infarction with a secondary infiltration of the wall of the appendix with inflammatory cells. Thrombosis of blood-

7. Aschoff: Die Wurmfortsatz Entzündung, 1908, p. 8.
8. Obendorfer: Ergebn. d. Allg. Path. u. path. Anat., 1909, xiii, 1, p. 553.

vessels elsewhere in the body has been observed at times in marantic infants; such a condition of the renal vessels is not uncommon. The condition of thrombosis in the appendices of these infants, as in the adult appendicitis, is probably the result of the blood-vessels of the appendix sharing in the adjacent inflammation. The inflammatory changes that are obvious, occur chiefly in the muscularis and serosa. The presence of polynuclear leukocytes, lymphocytes, and occasionally eosiniphils, in a moderately edematous muscularis and in the strikingly edematous serosa, is the usual microscopic finding. The changes near the mesentery are perhaps most marked. The lymph-vessels are greatly distended with leukocytes and lymphocytes. The blood-vessels are greatly engorged and show the presence of many leukocytes and lymphocytes close to the intima, and in some cases actual thrombi. Sections of adjacent lymph-glands made in several cases, gave the usual microscopic evidence of acute inflammation.

It is of interest to note that the sections of the wall of the cecum or ascending colon made near the origin of the appendix, in only two instance in 200 cases showed inflammatory changes involving the intestinal wall. In both the cases the appendix was the site of inflammation. Hyperemia and hemorrhages into the mucosa occur not infrequently in these sections of the intestinal wall and at times small superficial necroses. In one case necrosis was seen in a lymph-follicle.

A hematogenous origin of appendix inflammation in such young infants is not probable. The early histologic picture in such infection in the adult appendix, according to Kretz,[9] consists of small bacterial emboli seen in the capillaries of the lymph-follicles, together with small adjacent hemorrhagic exudates. Such lesions could not be demonstrated in the appendices described above.

Congenital syphilis was not found as an associated lesion in any of the fifteen infants. In two infants in whom congenital syphilis was believed to be a possible condition, based on the history obtained, the histologic findings in the viscera were entirely negative, and the *Spirochæta pallida* could not be demonstrated in the liver.

The extension of inflammation through a possible infection of the genital tract, as in Case 2, could be excluded by the microscopic findings. The serosa of the uterus and that of both tubes appeared intensely inflamed, while the muscularis and the mucosa were quite normal.

The cause of the inflammation must be sought for in the intestinal tract. In all probability the inflammatory changes in the appendices of young infants dying from malnutrition may be construed as a final infection of the appendix occurring in the later stages of a general infection of the gastro-intestinal tract.

9. Kretz: Verhandl. d. deutsch. path. Gesellsch., 1910, p. 147.

SUMMARY

1. Among 200 infants dying with gastro-intestinal symptoms and malnutrition, fifteen gave evidence at autopsy of inflammatory changes in the appendix.

2. The lesion occurred in infants whose ages ranged between 13 days and 2 months.

3. Peritoneal exudate was present in seven cases.

4. Thrombosis of the arteries occurred in the appendix and in the mesentery of the appendix in several instances.

5. The anatomic position of the appendix was found to influence the inflammatory changes.

6. The inflammatory changes in the appendices of young infants dying with symptoms of malnutrition occur probably as a result of a final infection of the appendices in the later stages of a general infection of the gastro-intestinal tract.

In concluding, I wish to express my obligations to Dr. John Howland for the privilege of performing the autopsies during his service as pathologist of the Foundling Hospital; and also to Dr. Eugene L. Opie, under whose direction the work was carried out.

PROGRESS IN PEDIATRICS

ANATOMY, PHYSIOLOGY AND HYGIENE

Continuous Function of the Mammary Glands

(*Moriz Schein: Wien. klin. Wchnschr., Sept. 22, 1910, xxiii, No. 38, p. 1337*)

Schein believes that the mammary gland produces an internal secretion, of which we have had up to this time no knowledge; the function of the mammary glands is not periodic, but continuous. In those periods when milk or colostrum is not secreted, he believes that a varying quantity of an internal secretion is being produced insensibly.

MAURICE OSTHEIMER.

BACTERIOLOGY AND PATHOLOGY

The Incubation Period of Serum Disease

(*F. Hamburger and R. Pollak: Wien. klin. Wchnschr., August 11, 1910, xxiii, No. 32, p. 1161*)

This forms the third communication made by the authors on this subject. After giving details of their experimental investigations, they conclude that there exists already, even during the incubation period of serum disease, a specific oversensitiveness to serum; and that this does not appear suddenly, but increases gradually in its intensity.

MAURICE OSTHEIMER.

Hemagglutinin Reaction in Serum Disease

(*Felix Bauer: München. med. Wchnschr., Jan. 10, 1911, No. 2*)

Bauer tried to get a serum reaction which would be specific for serum disease. Such a reaction must be present in every case of serum disease and must also be present after any injection of serum without any signs of serum disease. He found that after any injection of horse serum there is a production of agglutinins in the blood. The technic is simple, being like that of the Widal reaction, except that washed horses' red blood-cells are used instead of typhoid bacilli. Complete agglutination occurs in dilutions of 1 to 200, or more, in pronounced cases of serum disease. This reaction would be of use in making a differential diagnosis of the skin condition in serum disease and the exanthemata.

HERMAN SCHWARZ.

Influence of the Components of Breast-Milk on the Intestinal Flora of Sucklings

(*H. Bahrdt and A. H. Beifeld: Jahrb. f. Kinderh., lxxii, Supplementary No. 71*)

The authors, after reviewing the literature on *B. bifidus* and the intestinal flora of infants, report the results of microscopic examinations of stools of infants fed on various modifications of breast-milk, by which the influence of each constituent—fat, proteid, sugar, and salts—by its presence or absence, could be observed on *B. bifidus* of Tissier, present in the normal stool of the breast-fed infant, to the practical exclusion of all other organisms. Both centrifugalized human-milk, and breast-milk to which human-milk cream had been added produced stools in which the microscopic picture was identical with that of the breast-fed infant. This indicated that the fat played a minor rôle in determining the presence of *B. bifidus* in the stool. A suspension of human milk-curd in water, however, caused a disappearance of the *B. bifidus* flora, which was replaced by

the mixed—Gram-positive and negative—flora seen usually when cow's-milk mixtures are given. The whey, on the other hand, caused the reappearance of the bifidus flora, the same microscopic picture persisting after feeding a suspension of curd in a whey diluted with an equal part of water. The curd suspended in a still more dilute whey—three-fourths water—again permitted a large number of Gram-negative organisms to make their appearance. Suspensions of human as well as of cow's-milk curd in a 6 per cent. lactose solution gave a typical breast milk stool, with the corresponding bifidus flora. The conclusion is drawn that lactose is that constituent of human milk which is responsible for the exclusive presence of *B. bifidus* in the stools of the breast-fed infant. This is due to the fact that the relatively large quantity of this sugar, as against the slight amount of proteid, favors the normal fermentative process in the small intestine, the acid products of which (i. e. lactic acid) inhibit the growth of Gram-negative putrefactive bacteria, such as *B. coli*, which would flourish were the proportion of carbohydrate and proteid reversed. The Gram-positive bacteria such as *B. bifidus* and *B. acidophylus* are not checked in growth by the acid medium.

G. L. MEIGS.

METABOLISM AND NUTRITION

Cretinism Among Jews

(*Arnold Flinker: Wien. klin. Wchnschr., Dec. 29, 1910, xxiii, No. 52, p. 1871*)

Flinker found fourteen cases of, apparently, endemic cretinism in Wiznitz, occurring among the Jews of the vicinity. He describes four of the patients in detail, with photographs. At the same time several cases were also found among others living in the neighborhood. While endemic goiters appeared in the first generation of settlers, cretinism was found in the second generation. No other children in the families of these children developed the disease, even though they lived and slept with the cretins all their lives. Flinker concludes that cretinism cannot, therefore, be contagious.

MAURICE OSTHEIMER.

Nitrogen and Sulphur Metabolism in Rachitic Dwarfism

(*Herman Schwarz: Jahrb. f. Kinderh., 1910, lxxii, Series 3, xxii, No. 5*)

In the normal metabolism of a 5-year-old child, seventy calories per kilo weight was enough to cause an increase in weight in the seven-day experiment. In the first case of rachitic dwarfism, ninety-four calories per kilo, in the second case, ninety-four calories per kilo, and in the third case eighty-three calories was sufficient to keep them in nitrogen equilibrium and slightly increase their weight. The nitrogen resorption was 90 per cent. in the normal case, 93 and 96 in cases 2 and 3, and only 80 per cent. in case 1. The total nitrogen excretion in the urine in the normal case was 74 per cent., 72 per cent in case 1, 78 per cent. in case 2, and 81 per cent. in case 3. During a period of fever in case 2, the nitrogen excretion was increased. The ammonia nitrogen coefficient was about the same in all cases. During an attack of urticaria in case 1 the ammonia excretion was slightly increased, and during the fever attack of case 2 it was greatly increased. Uric acid nitrogen in the normal case was about 83 mg. per day, less in cases 1 and 2, and much less in case 3. The creatinin nitrogen excretion in the normal child was about 150 mg. The creatinin nitrogen coefficient was about 6.8. In cases 1 and 2 the creatinin was distinctly diminished, the coefficients being 5.9 and 2.4. This decrease might be due to a diseased condition of the liver. Creatin was not present in the normal case. In cases 1 and 2 the amount of creatin was often as much, if not greaer than, the creatinin. This might be due, first, to a diseased condition of the liver (Mellanby), and second, to the condition of the musculature in these cases of rickets (Hagenbach-Burchardt and Bing). In case 3, in which the liver was normal in size and the child's locomotion

normal, there was no creatin excreted. The sulphur metabolism showed a resorption of 92.2 per cent. in the normal case, 76 per cent. in case 1, and 83 per cent. in case 2. The retention was 31 per cent. in the normal case, 30 per cent. in case 1, and 26 per cent. in case 2. The total sulphur excreted in the urine was 61 per cent. of the intake in the normal case, 55 per cent., 54 per cent. and 54 per cent. in cases 1, 2, and 3, respectively. The amount of sulphur in the feces was 7.8 per cent. of the intake in the normal case, 23 and 17 per cent. respectively in cases 1 and 2. HERMAN SCHWARZ.

Two Methods of Obtaining Human Milk for Hospital Use

(Fritz B. Talbot: Boston Med. and Surg. Jour., 1911, clxiv, 304)

The author describes the methods used to procure breast-milk at the Massachusetts Infant Asylum and the Boston Floating Hospital. At the former institution there are resident wet nurses, obtained from lying-in hospitals and other charitable institutions. These women take entire care of their own babies and do some light work. The milk of these wet nurses is used in two ways: (1) The milk is drawn with breast pumps for the very weak and delicate babies; (2) the stronger babies are put on the breast. The women are paid according to the amount of milk they supply, at the rate of two cents an ounce for "drawn milk" and one cent an ounce for nursed breast milk, up to a limit of sixteen dollars a month. Each woman gives about one quart daily. The average duration of residence in the hospital is six to eight months.

At the Boston Floating Hospital breast-milk was obtained by a trained nurse from nursing women in the tenement district who had a superabundance of milk. Mothers willing to supply milk were examined by one of the physicians of the hospital for signs of tuberculosis or syphilis. Each woman's family physician was then required to sign a card stating that in his opinion it would do no harm for the woman to supply this milk. The women were paid at the rate of sixty cents a quart but the movement became so popular that many of the mothers were unwilling to accept any recompense. RICHARD M. SMITH.

Technic of and Indications for Feeding Albumin Milk

(H. Finkelstein and L. F. Meyer: München. med. Wchnschr., Feb. 14, 1911, No. 7)

After describing the general procedure adopted at the Kinderasyl, Finkelstein and Meyer lay down the following rules to be observed in giving eiweissmilk:

1. The eiweissmilk must not have any lumps and on shaking should be of homogeneous consistency. From the start there must be at least 1 per cent. of carbohydrate, best in the form of a malt sugar.

2. In dyspepsia and atrophy (decomposition) a cathartic should be given, six hours tea diet, and then eiweissmilk in no smaller dose than 300 gm. a day—to which in most cases the 1 per cent. carbohydrate has been added. This is increased rather rapidly so that the child is given 180 to 200 gm. per kilo weight regardless of the character of the stools or other conditions. Should the weight not stop decreasing in the course of a few days, the carbohydrate must be increased to 2 to 3 per cent., especially when subnormal temperature and collapse occur. If the above named dose has been reached and there is no increase in weight, the carbohydrate is to be increased to 3, 4 or 5 per cent., or flour may be added instead. Many children do not gain until 6 or 7 per cent. carbohydrate has been added. As carbohydrate, dextrin-maltose preparations or flour alone or in combination are preferred.

3. Carbohydrate may be added even when the stools are numerous and watery up to 3 per cent. and, under close observation, even higher than this.

4. Under no circumstance should the carbohydrate be reduced below 2 or 3 per cent. when adding the carbohydrate has once been started.

5. Should untoward results occur during the administration of the eiweisswilk and the weight not decrease too rapidly, do not stop it but wait. Usually spontaneous improvement occurs. It is advisable to cut down the carbohydrate percentage slightly if it happens to be over 4 per cent. If marked decrease in weight

occurs it is best to cut down the amount of eiweissmilk from 150 to 200 gm. per diem and the carbohydrate to 2 or 3 per cent. All in all, until the intercurrent infection has disappeared it is best to give a little less than the 180 to 200 gm. per kilo and to stick to the 3 per cent. carbohydrate.

In enterocatarrh and cholera infantum they advise tea diet for twelve to twenty-four hours; then ten times, 5 to 10 gm. eiweissmilk and tea for the next twenty-four hours; then 50 gm. eiweissmilk are added daily until marked diarrhea has stopped; then a rapid increase to 180 to 200 gm. per kilo weight.

At this time they begin increasing the carbohydrate; should, however, the decrease in body weight not stop after three or four days of the treatment, the carbohydrate should be added earlier. In very toxic cases the above scheme should also be carried out. After giving 130 to 150 gm. eiweissmilk with 3 per cent. carbohydrate, one can wait until all toxic symptoms have disappeared. To try to reduce the toxemia by continued starvation is an error and can cause death. In conclusion they expressly state that no other nourishment should be given during the eiweissmilk therapy. Not even woman's milk should be added. In mild cases the addition of woman's milk has seemed to be without harm, but in serious cases it was distinctly deleterious. HERMAN SCHWARZ.

ACUTE INFECTIOUS DISEASES

The Spread of Scarlet Fever

(*Heinrich Kokall: Wien. klin. Wchnschr., Dec. 29, 1910, xxiii, No. 52, p. 1874*)

Kokall relates histories of twenty instances of "return" cases of scarlet fever occurring just as soon as the apparently well child mingles with other children, in spite of disinfection repeated several times, isolation in the hospital, and even longer separation from the family and friends. He believes that disinfection is of no value in preventing these "return" cases; that the patient alone is the infecting agent, even for a long time after his attack; certainly longer than six weeks afterward. Therefore, efforts should be made to keep the mouth free from germs before letting a child out of quarantine. But no certain method has yet been found, nor will be, probably, so long as the exciting cause of scarlet fever remains unknown. MAURICE OSTHEIMER.

Antityphoid Inoculation as Introduced into Certain Training Schools for Nurses

(*Mark W. Richardson and Leslie H. Spooner: Boston Med. and Surg. Jour., 1911, clxiv, 8*)

The authors report the inoculation of physicians, nurses and ward-tenders at the Massachusetts General and nine other hospitals in Massachusetts. This work was undertaken because from previous investigations it was concluded that "the hospital nurse in Massachusetts is about eight times as liable to contract typhoid fever as the ordinary citizen." Four hundred and five individuals were given 1,588 inoculations. There were no untoward results. At the Massachusetts General Hospital for the ten years previous to 1909 from two to six nurses had typhoid fever each year. In 1909 and 1910 there were no cases of typhoid fever among nurses in that institution. The authors believe that the inoculated individuals have acquired an increased resistance to typhoid infection which will last them for several years. RICHARD M. SMITH.

TUBERCULOSIS AND SYPHILIS

Diagnosis of Tuberculosis of the Bronchial Glands

(*Henry F. Stoll. Am. Jour. Med. Sc., January, 1911*)

The author gives a careful résumé, with citation of authorities of the significant symptoms and physical signs leading to a diagnosis of this condition.

The points on which different observers lay greatest stress are: tenderness over the spines of the upper thoracic vertebræ; dullness over the fifth or sixth dorsal spines; paravertebral dullness, best elicited by light percussion; bronchophony downward over the thoracic spines for a variable distance, at times present only over the fifth; crepitant râles in the fourth, fifth and sixth interspaces at about the mid-clavicular line, and radiography. He points out the importance of a tuberculin test if one or more of the above signs are present. The author insists on the importance of early diagnosis as tuberculin therapy is most efficacious in glandular tuberculosis. The cases studied by Stoll were mostly in older children but he considers the points of diagnosis equally applicable to infants.

FREDERIC H. BARTLETT.

The Splenomegaly of Inherited Syphilis

(*F. P. Weber: Proc. Roy. Soc. Med., 1911, iv, 67*)

Weber sums up his conclusions in regard to splenomegaly in children and inherited syphilis, from a study of the literature and six of his own cases, as follows: 1. Moderate splenomegaly in children from the ages of 5 to 16 may be almost the only evidence of an inherited syphilitic taint, but in such cases the Wassermann test would doubtless give a positive result. Other evidences of inherited syphilis are occasionally forthcoming, as Hutchinson teeth, interstitial keratitis, cracks at the corners of the mouth, a history of skin eruptions in babyhood, a history of syphilis in the parents, inherited syphilis in brothers and sisters, etc. 2. It may be accompanied by occasional slight attacks of jaundice and by excess of urobilin and urobilinogen in the urine. 3. Hepatic cirrhosis. 4. Infantilism—more or less retardation in physical development, especially in the sexual function. 5. In certain cases, a polycythemia, probably of a reactive nature. 6. Abdominal crises of uncertain explanation. Familial splenomegaly, occurring in two or more brothers or sisters. 7. Some cases present the symptoms of splenic anemia or Banti's disease.

J. B. C.

Pemphigus Syphiliticus of the New-Born

(*Prof. Baisch: München. med. Wchnschr., Jan. 31, 1911, No. 5*)

Baisch describes a case of pemphigus syphiliticus which was observed in the Kgl. Universitats Frauenklinik, München, and points out the bad prognosis in this form of congenital syphilis, even if given mercurial treatment. The spirochetes are always found in the serous contents of the bullæ and are more easily stained with carbol water gentian-violet than with Giemsa. The child was literally covered with pemphigus lesions, weighed 2,450 gm., and was 46 cm. long. Since Taege (*München. med. Wchnschr.*, 1910, No. 33) and Dubot (*München. med. Wchnschr.*, 1910, No. 35) pointed out the good effect on the infant of the injection of salvarsan into the mother, he injected 0.4 gm. into the cubital vein of the mother on the first day post partum. The mother nursed the child on the fourth day, yet during these days the lesions in the child did not increase. On the seventh day, however, many new bullæ appeared. On the eighth day the child received 0.15 gm. salvarsan in the gluteal region. The result was excellent; for on the ninth day the lesions had almost all dried up and the child increased in weight. On the eighteenth day new pemphigus lesions appeared and the child received another dose of 0.15 gm. These new lesions promptly disappeared and the child continued to gain weight and appeared perfectly well on the fortieth day.

HERMAN SCHWARZ.

The Effect of Ehrlich's Salvarsan On Lues in Children, Especially on Congenital Syphilis

(*Richard Kalb: Wien. klin. Wchnschr., Sept. 29, 1910, xxiii, No. 39, p. 1378*)

Kalb reports the histories of eight children, two of whom had acquired syphilis, while six had hereditary syphilis. At first he employed small doses of salvarsan in neutral suspension, injected into the gluteal region. Later he used it in solu-

tion, supplied in sterile ampullæ. All the children stood the injections well, without pain or infiltration following. One child was suffering from Parrot's pseudoparalysis; another had great enlargement of the liver. Recovery occurred in the two children with acquired syphilis exactly as it occurs in adults. Mucous patches disappeared first, followed by the eruption, and last to go were the enlarged glands. In congenital syphilis the eruption disappeared first, then the bony changes and pseudoparalysis. While coryza may disappear rapidly, it may also persist for some time. In one child a defect of hearing improved very rapidly also. Kalb advises giving salvarsan to the nursing mother for its effect on the baby. He concludes that not only is salvarsan a more certain and more rapid therapeutic agent than any of the older methods of treating syphilis, but it may readily be employed in treating atrophic infants with severe gastric catarrh; it seems to increase body weight and improve the general condition of the infant.

MAURICE OSTHEIMER.

An Examination of Scrofulous Children by Means of the v. Pirquet and Wassermann Tests

(R. Hertz and O. Thomsen: Berl. klin. Wchnschr., xliii, No. 6)

The object of this work was to more surely establish, by means of a specific reaction, the fact that tuberculosis is a dominating factor of etiology in scrofulosis. Of 228 cases, 84 per cent. reacted positively to the v. Pirquet test, and 16 per cent. were negative. As all the cases were admitted to the Kysthospital for tuberculous surgical affections, this percentage is not remarkable; of the remaining 16 per cent., however, operation or autopsy proved the majority to be not tuberculous.

Wassermann tests on the 228 cases reacted positively in eight cases, of which four were only weakly positive; these four were later retested, and gave the same result. Three were evidently tuberculous, and one rachitic. These weak reactions showed only partial checking of hemolysis, and the same result was shown when the test was repeated several weeks later. Whether this meant luetic infection (congenital or acquired) must remain undecided, for such weak reactions have been known to occur in cases in which lues could most probably be excluded.

The mothers of these eight children denied all knowledge of having been infected with lues, and three of them were tested, with negative result; these three were manifestly tuberculous. Four showed marked positive reaction, and their children were given antiluetic treatment; undoubtedly in their cases the lues was the more serious factor of the illness; the marked Wassermann reaction, and the almost miraculous response to mercurial treatment, were clear.

Here is shown again the common experience, that the Wassermann test in congenital lues remains obstinately positive, even when combated vigorously with mercurials, and even if all symptoms disappear—a contrast to the behavior of acquired lues.

A. C. SOPER, JR.

BLOOD AND CIRCULATORY SYSTEM

Arterial Rigidity in Children

(Franz Hamburger: München. med. Wchnschr., Jan. 31, 1911, No. 5)

Hamburger says that the temporal or radial artery should not be felt normally either in the adult or the child. He finds them often palpable in children above the sixth or seventh year—sometimes as young as the third year. At times they are so marked that one might think of an arterial sclerosis or a kidney condition, but there is no anatomic evidence of the former and no clinical evidence of the latter. Careful examination of these children show them to be of a neuropathic type. They complain of headache, cardiac palpitation, migrain, and vasomotor disturbances, such as cold hands and feet. He often finds a pulsus irregularis respiratorius.

HERMAN SCHWARZ.

Splenic Anemia

(*A. Longo: Médécine des Enfants, December, 1910*)

Longo has had in his clinic at Catane a boy 17 months old suffering from splenic anemia. Both of his parents are healthy; three other children living and well; one brother died. The boy was born at full term; was breast fed, and after the tenth month weaned. When 16 months old (middle of January) he suffered from green diarrhea, fever and pallor. The large spleen, somewhat enlarged liver, temperature and pulse of 124 at first suggested Malta fever. On February 19 the child was worse, looked extremely pale, and had gingivitis, with fetid breath. He died February 27, forty days after the onset of the disease. On February 20 the spleen was punctured and corpuscles of Leishman were found. Blood-count the same day showed, red cells 3,800,000; leukocytes 16,000. Serum tests for typhoid, paratyphoid and Malta-fever were negative.

J. BLECHSCHMIDT.

Infantile Splenic Anemia

(*G. Zamboni: Médécine des Enfants, December, 1910*)

In his article published in *Riv. di Clin. Pediat.* (July 10, 1910), Dr. Guiseppe Zamboni expresses it as his opinion that there is a fundamental difference between splenic anemia and kala-azar (Leishman). He refers to twelve of his patients treated at the pediatric clinic of Dr. C. Comba in Bologna.

These cases—several of which were treated by *x*-rays—showed the following variations in blood-counts: red cells, from 1,500,000 to 3,940,000; leukocytes, from 3,000 to 34,500. Pallor and splenic enlargement were dominant features, but fever was not constantly observed. (In kala-azar fever is present and a slight icterus usually accompanies it). Of his twelve patients, six died, two were cured (?), one slightly improved, one was of the adult form, two had unknown terminations.

Out of 146 published cases ninety-nine were boys, forty-seven were girls. Of the twelve cases of Zamboni seven were boys and five were girls. As to age, fifty-seven were 1 year or under; between 1 and 2 years, sixty-five; over 2 years, twenty-four. Of Zamboni's patients four were 1 year or under; seven were between 1 and 2, and one was over 2. The predominance of the disease in early life seems to point toward digestive disturbances as an etiologic factor. To this there must be added according to the author, congenital syphilis, maternal diabetes, anemic predisposition running in families, rickets, enlarged bronchial glands, malaria, measles and suppurative foci. As regards pathogenesis, the spleen is of primary importance and by acting on it, *x*-rays combat the anemia. In none of his cases has Zamboni been able to discover the parasites of Leishman.

J. BLECHSCHMIDT.

Hemophilia and Blood Coagulation

(*Max Vogel: Ztschr. f. klin. Med., 1910, p. 224*)

Vogel reports a case of hemophilia in a 10-year-old boy in whose family for three generations back no history of hemophilia could be traced. The parents of the boy were blood relations (cousins). At 6 months of age he suffered from a subcutaneous hemorrhage. When 11 months old he received a slight injury to the frenum of the tongue, which was followed by hemorrhage that lasted eleven days, and it was at this time that the diagnosis was made. At various times it was noticed that slight injuries caused marked hemorrhages, external or subcutaneous. In 1907, hemorrhages into the knee and ankle joints were first noticed. Since this time the general health declined and there were also hemorrhages into both knees. The patient became bedfast; every attempt to arise being associated with severe pains and copious hemorrhages into the knee-joints. The boy was under Vogel's care for about a year and a half, during which time there had never been any hemorrhage into the mucous membranes. Nov. 20, 1909,

the boy's condition was especially marked by lameness from the affection of both knees. His development indicated a fairly well nourished boy (weight not stated). The skin and mucous membranes were somewhat pale. On the left temple there was a prominent scar (4x3 cm.). Other scars were found on front of the left thumb, and on the lips. There was a subcutaneous hematoma in the right popliteal space. Both knee-joints were considerably swollen and fluctuating and were painful on motion. Radiographs showed normal bones; there was no edema; temperature, heart and lungs normal; urine without special interest; liver and spleen normal; a few indolent glands the size of hazel nuts, in the inguinal region. Hgb. 70 per cent.; r. b. c. 5 million; whites 8,500. Since November 9, the condition of the boy did not change materially and he had been unable to leave his bed. About the joints, spontaneous hemorrhages would occur, here and there.

This condition should be differentiated from congenital hemophilia, in which there is bleeding from the mucous membranes and internal organs (nose, kidneys, bowels, etc.). It may also be added that the progress of the hemorrhagic lesions in this case was very slow.

The coagulation of the blood was tested by Vierordt's and Morawitz's methods. By Vierordt's method, normal blood coagulates in four hours; hemophilic blood in thirteen hours ten minutes. By the Morawitz method normal blood coagulates in five hours thirty minutes; hemophilic blood in eighty-eight hours and forty-five minutes.

The blood of three brothers of this patient was tested by the Vierordt method and gave the following results: (1) seven hours fifteen minutes; (2) seven hours forty-five minutes; (3) twenty-one hours twenty-five minutes. As a control test, the blood of a healthy stranger coagulated in seven hours twenty-five minutes. It is interesting to note that the third brother, although not a bleeder, had blood with hemophilic coagulation time.

Vogel made coagulation tests of the blood with various materials, as organic extracts, fresh serum, diphtheria antitoxin, calcium chlorid, phenol, glycocol, grape sugar and fresh human and rabbit's-blood. He found that a clot was readily obtained by adding human and rabbit's blood; with the other tests, the blood was still fluid after twenty-four hours.

By adding 2 c.c. rabbit-blood to 3 c.c. joint-blood a clot was obtained in seven hours fifty-five minutes, but by adding seven drops human blood to 2 c.c. joint-blood a clot was only established after sixteen hours thirty minutes. Very marked was the uselessness of the organic extracts. Under the impression that the result could be improved by adding lime salts to organic extracts, calcium chlorid and organic extracts together were tried, but again with absolutely negative results. A control test with normal blood and rabbit's blood proved the rapid, strong reaction, a clot being formed in fifty minutes.

Perhaps all these tests do not prove conclusively the correctness of Sahli's hypothesis concerning hemophilia. In conclusion Vogel considers this a new case of hemophilia in which clotting took place in eighty-eight hours (Morawitz-Bier method). Experiments with this method gave slight reaction with glycocoll. Sodium chlorid always acted slowly. Fresh-flowing rabbit's-blood always worked rapidly. Organic extracts also hastened very much the clotting of normal blood. In rabbits intravenous injection of organic extracts made very little impression. Hemophilic blood mixed with organic extracts under the same condition will flow after one hour like normal blood. Lastly, Vogel calls attention to the third brother of the patient, whose blood coagulation time was the same, although never having had any evidences of hemophilia. C. H. LEFCOE.

Splenic Anemia a Parasitic Disease

(*R. Jemma: Médécine des Infants, December, 1911*)

Italian pediatricians (Cardelli, Somma, Fede) had for a long time considered splenic anemia as a disease distinct from other splenic enlargements. What their clinical observations led them to surmise has just been demonstrated with a cer-

tain precision by Dr. Rosco Jemma, professor of Pediatrics in the University of Palermo.

Searching for the parasite of Leishman in cases of splenic anemia he punctured the spleens of these patients, but was at first unsuccessful. Later, in May, 1909, he found the parasites in a boy aged 6. He was healthy up to his fifth year; the disease began in January, 1909, with fever preceded by chills and followed by sweats. The fever continued for three months and was irregular in every way; i. e., as to time of attacks, duration and intensity. In the beginning it was of the quotidian type; later it was absolutely irregular. There was nausea, dry cough, with pain in the left hypochondrium, headache, pallor of skin and mucous membranes, emaciation, no enlarged glands, but protruding abdomen, enlarged liver and spleen, the upper border reaching the eighth rib; the lower border 3 cm. below the transverse umbilical line. Blood-count May 1 was as follows: erythrocytes, 3,000,000; leukocytes, 16,000; hemoglobin, 65 per cent.

Puncture of the spleen in June gave a negative result. Tests for typhoid, paratyphoid, Malta fever and Koch's bacillus were all negative. The fever continued with light remissions and periods of the intermittent type to the end of August. Attempts were made to build the child up. X-rays brought some amelioration. The blood-picture September 20 showed: reds 3,987,000, whites 11,870, hemoglobin 65 per cent. October 3 another splenic puncture was made by means of a special trochar which allowed withdrawal of some of the splenic pulp. Preparations of this with Giemsa stain showed the corpuscles of Leishman, which the latter found and described in patients suffering from kala-azar in India, and which later on were found by Nicolle (Tunis) and by Pianese and Gabbi (Italy), in individuals attacked with splenic anemia. There can be no doubt that the enlargement of the spleen and all the other symptoms of the disease in this boy were due to these parasites. They were not found the first time because a Lüer syringe with an ordinary needle was used; the special trocar used the second time allowed some of the splenic pulp to be withdrawn. Jemma is convinced that many of the cases of infantile splenic anemia which he has observed in hospital and private practice are due to the parasites of Leishman. In an article in *Riforma medica* (1910) he has described six additional cases of infantile splenic anemia in which he was able to demonstrate the presence of the Leishman corpuscles after splenic puncture. It is remarkable that in one case he succeeded in inoculating a dog with it.

Sir Patrick Manson defines kala-azar as an infectious disease characterized by its chronicity and irregular fever, hypertrophy of the spleen and often of the liver, the presence of Leishman corpuscles in these and other organs, emaciation, anemia, frequently a peculiar pigmentation of the skin and a high mortality. Nearly all of these symptoms were found in Jemma's observations. The cases of kala-azar studied in India by Leishman and Donovan have often been attributed to malarial cachexia, but the corpuscles discovered by these two scientists have removed all doubts. In the human body these parasites are nearly always intracellular; they multiply in the invaded cell until it bursts and then they attack other cells. The disease is probably transmitted by the sting of an insect.

Kala-azar attacks both sexes, all ages, the natives as well as the new-comers—contrary to malaria. According to Roger there is only a moderate degree of anemia and there is leukopenia. In all the cases reported by Jemma there was slight leukocytosis. The inoculation of dogs was successful in Tunis (by Nicolle) and in Palermo (by Jemma); the corpuscles of Leishman were found in the spleen of these animals. Nicolle even thinks now that children might be infected by dogs. He has tried to prove the existence of a spontaneous infection of "Leishmania" in the Tunis dogs. Post-mortem examination of twenty-five dogs showed corpuscles of Leishman in four of these animals. Therefore, in Tunis, kala-azar might be of canine origin.

Following in the steps of Nicolle, Dr. Jemma examined the spleen of 170 dogs in Palermo with negative results. However, the parasite of Sicily has been identified by Dr. Nicolle with that of Tunis. The kala-azar of Palermo is there-

fore the same disease as that of Tunis. The cultures of the parasite on different media, especially agar, have given positive results (although very slowly and with difficulty). The conclusions are as follows:

There is no doubt that there exists in Palermo as in Naples, Messina, Catane, an infectious disease caused by a parasite which by its morphologic and cultural characteristics resembles that which Leishman has found in Indians attacked with kala-azar. But we cannot yet admit the identity between the Indian kala-azar and the infantile splenic anemia of Tunis or Sicily. In India the kala-azar (or dum-dum-fever) takes an epidemic or endemic form and has a high mortality. In Italy splenic fever or splenic anemia—although considered an infectious disease by different authorities (Fede)—has never shown an infectious or epidemic character. In India kala-azar attacks all ages; in Italy splenic anemia is limited to young children. The cutaneous pigmentation of Indian kala-azar is not seen in infantile splenic anemia. In India the disease develops with a fever more or less intense, lasts some months, is nearly always fatal. In Italy it is sometimes without fever, may persist for several years, and often ends in recovery.

Nicolle and Jemma have been able to raise the parasite on agar; in India it grows only on a specially prepared blood-serum. In Italy and Tunis it is inoculable in dogs; in India it is not. Therefore, for the present one cannot consider that these two diseases are identical.

Pianese, who was the first to show in Italy the presence of Leishman corpuscles in infantile splenic anemia, continues to distinguish two forms of the disease: (1) The parasitic form, due to Leishman's corpuscles; (2) that due to different causes, such as syphilis, tuberculosis, malaria and diseases of nutrition.

One must understand that infantile splenic anemia (so well described by Cardarelli, Somma, Fede) is a primary disease which has nothing to do with syphilis, tuberculosis or malaria. From now on one ought to reserve the name of splenic anemia for the disease characterized by the presence of Leishman's corpuscles. The other varieties ought to be called splenomegaly with secondary anemia due to syphils, tuberculosis and malaria.

Kala-azar, says Dr. Jemma in closing, is a tropical disease which has nothing to do with our infantile splenic anemia, although the causal protozoa of these two diseases have very similar morphologic characteristics. We leave the exotic term (kala-azar) to the Indian disease and continue to call the other disease splenic anemia, under which name it has been known and described for generations.

J. BLECHSCHMIDT.

GENITO-URINARY DISEASES

A Superfluous Ureter

(*Robert Cristofetti: Wien. klin. Wchnschr., Oct. 27, 1910, xxiii, No. 43, p. 1510*)

Cristofetti reports an interesting case of a girl aged 15, who had been treated for years unsuccessfully for incontinence of urine. He found that she had a third ureter which opened into the vagina. After trying unsuccessfully to operate through the vagina, he finally performed laparotomy, found the dilated extra ureter lying close to the normal left ureter, dissected it free and inserted it into the bladder anterior to the normal ureter. Cystoscopic examination four weeks after the patient had left the hospital showed urine entering the bladder through all three ureters.

MAURICE OSTHEIMER.

Infections of the Urinary Tract by Bacillus Coli in Infancy and Childhood

(*C. R. Box. Pediatrics, xiii, No. 1*)

In discussing infections of the urinary tract by the colon bacillus, Box summarizes treatment as follows: 1. The administration of sufficient potassium

citrate to make and keep the urine permanently alkaline. 2. Treatment by urinary antiseptics. 3. Treatment by serums and vaccines. In cases with acute local symptoms potassium citrate, administered in doses of 10 to 20 grains three or four times a day, has been entirely effectual. Urotropin and its allied antiseptics of the formalin group, also ammonium benzoate, sodium salicylate and boracic acid, were most disappointing, particularly in the chronic persistent cases. Serums were not needed in the acute cases. No permanent improvement was noted in the two chronic cases in which the patients were treated with autogenous vaccines, but incidentally it was discovered that washing out the bladder with the serum instead of urinary antiseptics produced a marked though temporary diminution in the number of bacilli present. HENRY F. KEEVER.

Method of Collecting Urine from Female Infants

(Charles H. Lawrence, Jr.: Boston Med. and Surg. Jour., 1911, clxiv, 309)

The method described is as follows: In a strip of adhesive tape, 2x6 inches, cut a hole a little larger than the vulval orifice of the infant from whom the specimen is to be obtained. The end of the strip which is to be applied posteriorly is split into two tails. A rubber glove thumb, cut off close to the glove, is dropped, tip first, through the hole in the strap, the adhesive side of which is held uppermost. That part of the rubber thumb which remains above the hole is turned down on to the adhesive surface of the strap and pressed firmly against it, care being taken to have the rubber flange narrow enough so that there will be a band of adhesive surface around it. The tip of the thumb is cut off, a test tube inserted and the joint made tight by wrapping it with adhesive tape. To apply the apparatus the strap is placed over the perineum so that the opening in it lies over the vulva, the anterior end extends up on to the lower abdomen while the posterior tails are directed backward and outward over the buttocks.

RICHARD M. SMITH.

Undeveloped Testicles

(Joseph Kyrle: Wien. klin. Wchnschr., Nov. 10, 1910, xxiii, No. 45, p. 1583)

Kyrle has thoroughly examined testicles from 110 cadavers of boys under 18 years of age, thirty-nine of them from infants under 1 year of age. In thirty-one evidence of tuberculosis was found; twenty-nine of these having died under 9 months of age. Of the 110 individuals, eighty-six were decidedly undeveloped; of the rest, twenty-four did not show normal development for the age of the boy. Of the thirty-nine infants under 1 year, twenty-nine had undeveloped testicles. Kyrle considers the presence of a large amount of intracellular connective tissue between the testicular canaliculi a good sign of undevelopment. The presence of other congenital anomalies in many of these cases substantiates the possibility of this undevelopment being congenital also. In others it may have been the result of chronic or infectious diseases. He believes that a large number of boys must be born with undeveloped testicles. The fact that so large a number of those dying in infancy had undeveloped testicles would lead one to conclude that, associated with this lack of development, there was also a decided lack of vital resistance. MAURICE OSTHEIMER.